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Journal of the Southern Medical Association

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Southern Medical Association, Forty-First Annual Meeting, Baltimore, November 24-26

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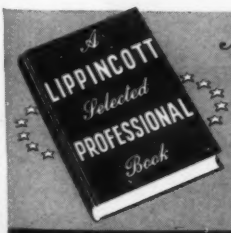

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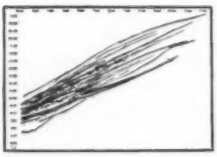

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2. Sikkema, S. H. and Sevringhaus, E. I.: Am. J. Med., *2*:251 (March) 1947.
3. Finkler, R. S. and Becker, S.: J. A. M. W. A., *1*:152 (Aug.) 1946.
4. Finkler, R. S. and Becker, S.: Am. J. Obst. & Gynec., *53*:513 (March) 1947.
5. Rakoff, A. E., et al: Clinical Evaluation of Dienestrol, A Synthetic Estrogen, Presented at Meeting of Assn. for Study of Int. Secretions, Atlantic City, N. J., June 6-7, 1947.
6. Gordon, E. S.: Value of Dienestrol in the Menopausal Syndrome (Tentative Title) to be published.

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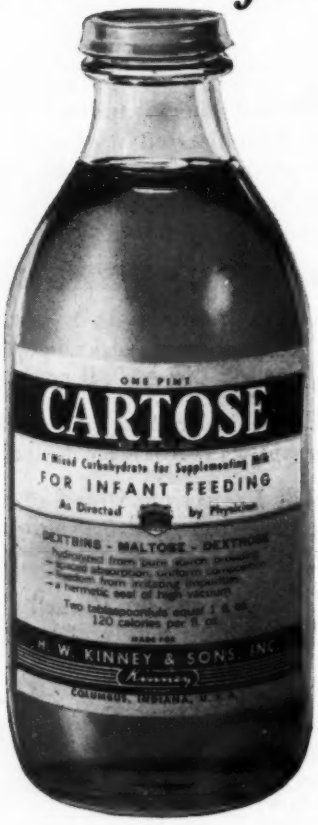

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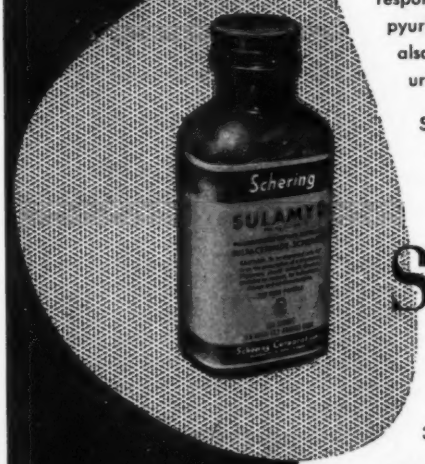

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AUTHOR

DeLor, C. J.; Means, J. W.; Shinowara, G. J., and Reinhart, H. L.: Rev. Gastroenterol. *8*:48 (Jan.-Feb.) 1941.

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Dolkart, R. E.: Illinois M. J. *87*:43 (Jan.) 1945.

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AUTHOR

Gauss, H.: Am. J. Digest. Dis. *12*:224 (July) 1945.

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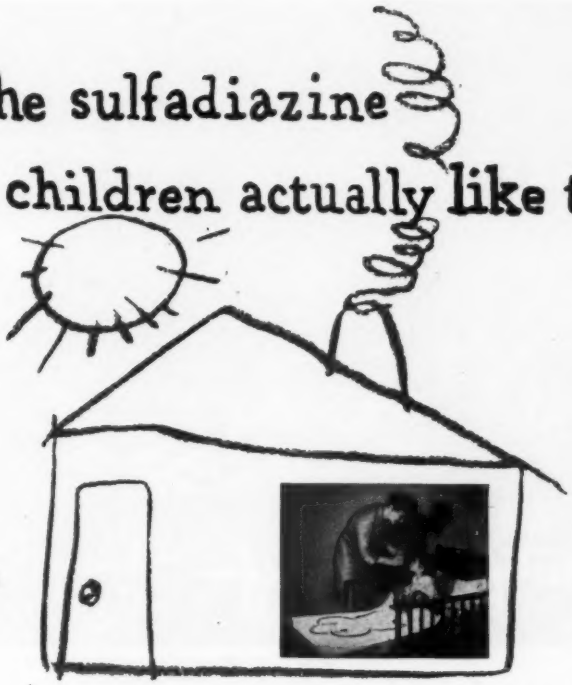

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*Am. J. M. Sc. 210:141, 1945

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In hepatic degenerative states requiring lipotropic support, let

Syrup CHOLINE Dihydrogen Citrate
(Flint)

solve your administration difficulties.

This surprisingly palatable preparation contains 25 per cent w/v of the choline salt. It may be taken over prolonged periods without taste objection.

Syrup Choline Dihydrogen Citrate (Flint) is supplied in pint and gallon bottles.

ACCEPTED AMERICAN MEDICAL ASSN. COUNCIL ACCEPTED

FLINT, EATON & COMPANY
DECATUR • ILLINOIS

BAXTER

Pioneer Name in Parenteral Therapy

● A Protein Hydrolysate Solution that is conspicuously reaction-free is another achievement of Baxter research. The perfecting of Protein Hydrolysate Baxter marks an important addition to Baxter's integrated parenteral therapy program . . . with its complete range of solutions . . . sets for separate or simultaneous infusions . . . its wide selection of simplified equipment for standardized procedures. No other method is used by so many hospitals.

★

Manufactured by
BAXTER LABORATORIES
Morton Grove, Illinois · Acton, Ontario

★

Distributed and available only in the 37 states east of the Rockies through...

AMERICAN HOSPITAL SUPPLY CORPORATION
NEW YORK • EVANSTON, ILLINOIS • ATLANTA • WASHINGTON, D. C.

area of agreement

Pediatricians and geriatricians agree upon the need for prompt control of cough because its effects are particularly exhausting upon the child and the aged.

DIATUSSIN

Bischoff

a non-narcotic antitussive achieves *cough control* speedily and pleasantly. Exceptionally palatable and safe as well as effective, DIATUSSIN is a preferred antitussive for cough in the young and the old.

Trade-Mark DIATUSSIN—Reg. U. S. Pat. Off.
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Printed U. S. A.

Bischoff

ERNST BISCHOFF COMPANY, INC. • IVORYTON, CONN.

FOR *Malaria*

A NEW DRUG OF CHOICE

ARALEN diphosphate (SN-7618) — the new synthetic, colorless, antimalarial specific which has been thoroughly investigated under the auspices of the National Research Council—has been demonstrated to be a very efficient antimalarial. It rapidly eradicates falciparum malaria and readily suppresses vivax malaria.

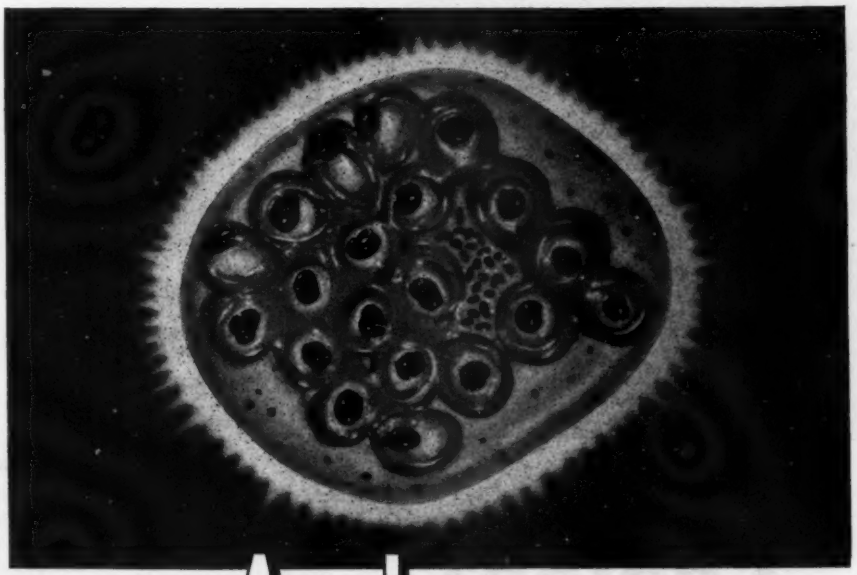
Only four doses administered over a three day period are required for the treatment of an acute attack: 4 tablets initially, 2 tablets after six to eight hours, and 2 tablets on each of two consecutive days. Aralen diphosphate is well tolerated. Being colorless it cannot cause skin pigmentation.

Tablets of 0.25 Gm., tubes of 10 and bottles of 100 and 1000 tablets.

Write for Informative Booklet

Winthrop CHEMICAL COMPANY, INC.

NEW YORK 13, N. Y. · WINDSOR, ONT.



Aralen diphosphate

Brand of chloroquine diphosphate

ARALEN, trademark reg.
U. S. Pat. Off. & Canada

Your patients get 2 kinds of relief with this new and different analgesic

It has been repeatedly demonstrated that amelioration of mood is a prime objective in the management of painful conditions.

EDRISAL presents a significant advance in the treatment of pain—in that it contains two recognized analgesics, *plus* the logical and effective anti-depressant, Benzedrine Sulfate. An increasing number of reports from physicians state that their patients prefer EDRISAL to other analgesic combinations.

This superior preparation affords prompt relief in a wide range of painful conditions, such as:

Dysmenorrhea
Simple headache
Neuralgia
Grippe
Sinusitis
Muscle and joint discomfort
Phlebitis
Rheumatism and allied conditions

Smith, Kline & French Laboratories, Philadelphia

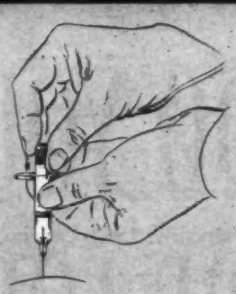
Edrisal *highly effective*

in the relief of pain

Real Convenience in Penicillin Therapy

1 The protective needle sheath is removed by a twisting motion, exposing the sterile 20-gauge needle. The sheath also serves as the syringe plunger.

2 Diaphragm end of cartridge is then dipped in an antiseptic solution and cartridge is inserted into syringe barrel just to point of inner needle.



3 Needle is now inserted into muscle into which injection is to be made and cartridge is withdrawn slightly to determine if needle end is in a vein.

4 If vein has not been entered, cartridge is forced into end of barrel lumen, causing inner needle to pierce cartridge diaphragm and to establish communication with the oil and wax mixture.

5 Plunger (needle sheath) is now inserted into cartridge. Pressure on end of plunger serves to expel contents of cartridge into muscle or subcutaneous tissue.

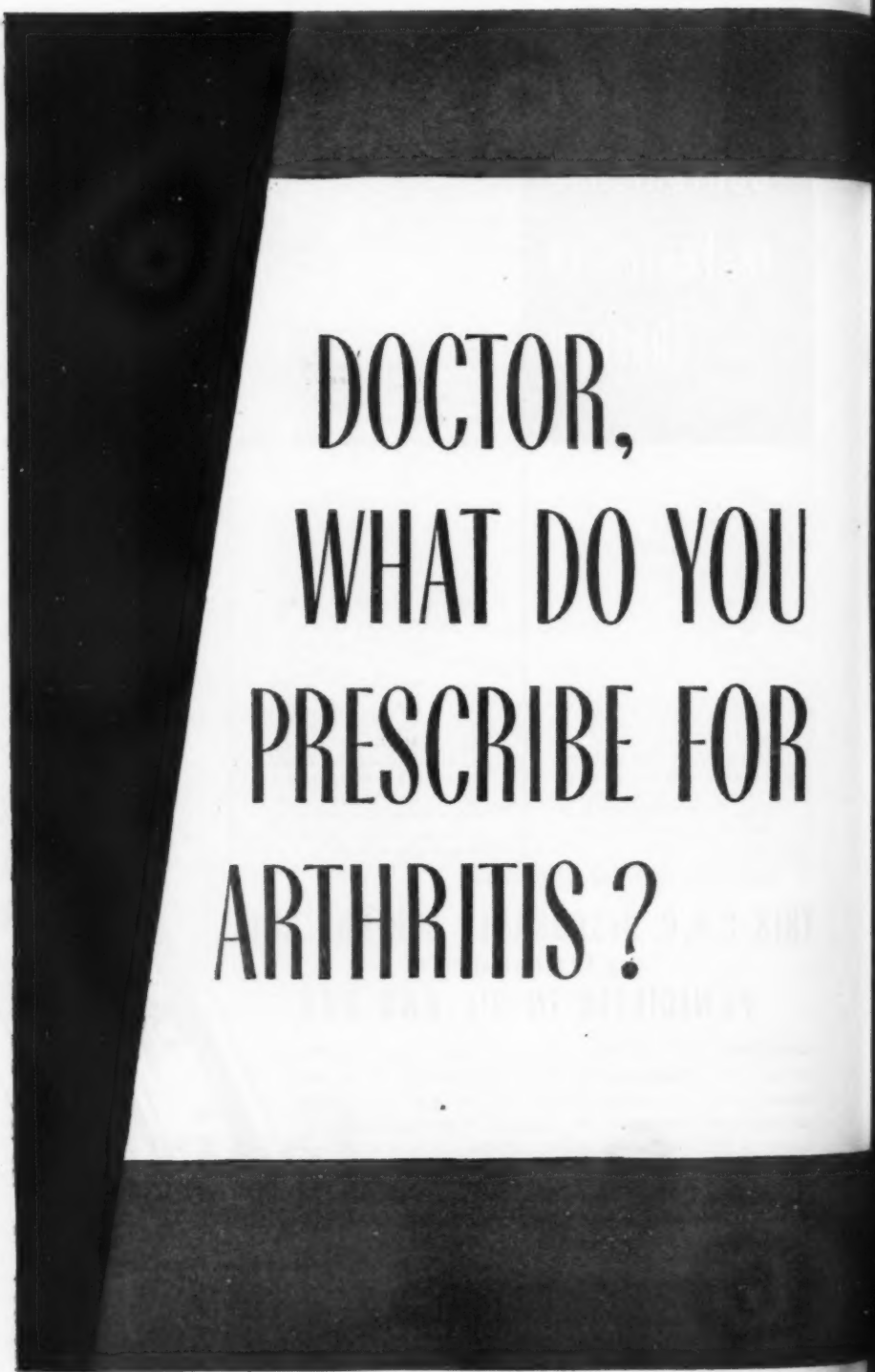
THIS C.S.C. DISPOSABLE SYRINGE UNIT
For Administration of
PENICILLIN IN OIL AND WAX

Administration of Penicillin in Oil and Wax is greatly facilitated by the C.S.C. Disposable Syringe Unit. Intended for a single injection only, this unique syringe and cartridge unit is sterile and ready for immediate use. Assembly is accomplished in a matter of seconds. The supplied cartridge contains a sufficient quantity of Crystalline Penicillin G Potassium in Oil and Wax (300,000 units per cc.) to assure injection of the full 300,000 unit dose. The illustrations show the simple technique of using the C.S.C. Disposable Syringe.

C.S.C. Pharmaceuticals

A DIVISION OF

COMMERCIAL SOLVENTS CORPORATION · 17 E. 42nd ST., NEW YORK 17, N. Y.


DOCTOR,
WHAT DO YOU
PRESCRIBE FOR
ARTHRITIS ?

ERTRON*

Steroid Complex, Whittier

There was a time when Arthritis could be considered hopeless. Today, as the literature shows, the gains made by Ertron over the dread disease have been outstanding. Ertron is the most widely prescribed anti-arthritic today.

*Reg. U. S. Patent Office

NUTRITION RESEARCH LABORATORIES

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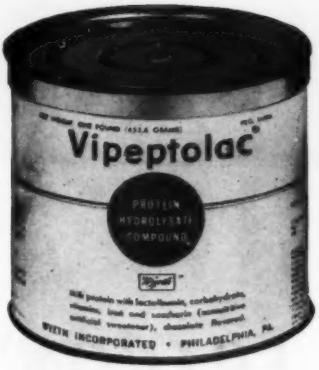
NOW



An amino acid product your patients will like to take

VIPEPTOLAC—A delicious chocolate-flavored protein food supplement. Vipeptolac combines amino acids, essential vitamins, iron and folic acid—*and it tastes good.* Mixed with milk or other liquids, Vipeptolac makes a delicious drink.

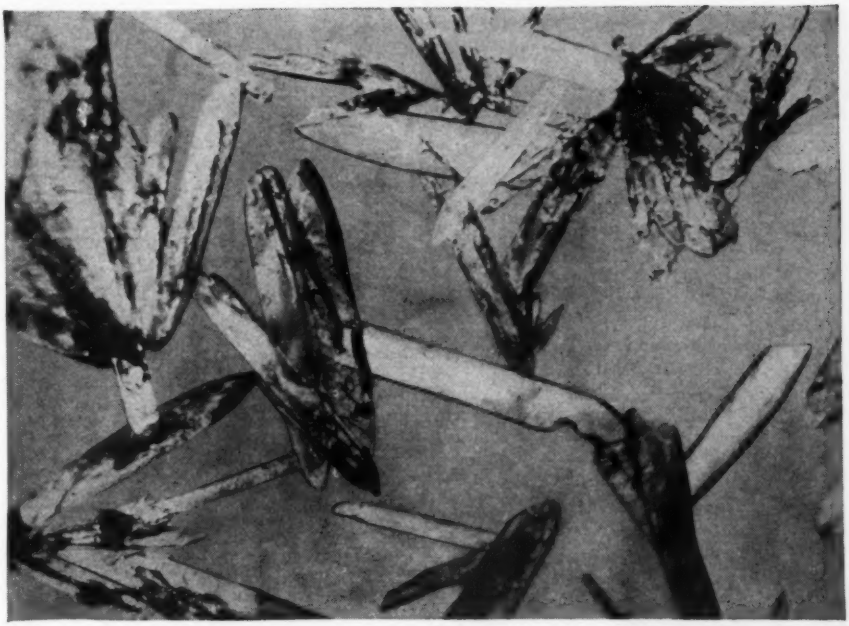
EACH 100 GRAMS OF VIPEPTOLAC PROVIDES:

Protein, polypeptides and amino acids (alanine, arginine, aspartic acid, cystine, glutamic acid, glycine, histidine, hydroxyproline, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophane, tyrosine and valine)	50 Gm.
Total nitrogen	7 %
Amino acid and polypeptide nitrogen	3.6%
Carbohydrate	37 Gm.
Fat	2 Gm.
Ash	9 Gm.
Calcium	1.2%
Phosphorus	1 %
Sodium	0.35%
Moisture	2 Gm.
Vitamin A	8000 U.S.P. units
Vitamin D	800 U.S.P. units
Thiamine Hydrochloride	6 mg.
Riboflavin	12 mg.
Niacinamide	60 mg.
Ascorbic Acid	60 mg.
Folic Acid	2 mg.
Iron (as ferrous sulfate)	25 mg.

VIPEPTOLAC®

Protein Hydrolysate Compound

WYETH INCORPORATED Wyeth **PHILADELPHIA 3, PA.**



Crystalline Penicillin G Sodium Merck—An Improved, Highly Purified Product

★ No refrigeration required for dry form.

★ Therapeutically inert materials which may act as allergens have been virtually eliminated.

★ Minimum irritation on injection as a result of removal of therapeutically inert materials.

★ Meets exacting Government specifications for Crystalline Penicillin G.

★ Penicillin G has been proved to be a highly effective therapeutic agent.

CRYSTALLINE
PENICILLIN G SODIUM
MERCK

MERCK & CO., Inc. RAHWAY, N. J.

Manufacturing Chemists

MERCK

Protection Through PLANNING

There is widespread agreement that fluorine is an important factor in preventing tooth decay. In "Enziflur" Lozenges, this substance is presented as calcium fluoride in combination with vitamins C and D . . . for the planned protection of the teeth against caries attacks.

"Enziflur" Lozenges should be allowed to dissolve slowly in the mouth in order to bring the fluorine-bearing saliva in prolonged contact with the surfaces of the teeth.

Descriptive literature outlining indications, dosages and contraindications available to physicians and dentists upon request.

"Enziflur" Lozenges (No. 805) are available in bottles of 30 and 100 each.

Ayerst

"ENZIFLUR"® *Lozenges*

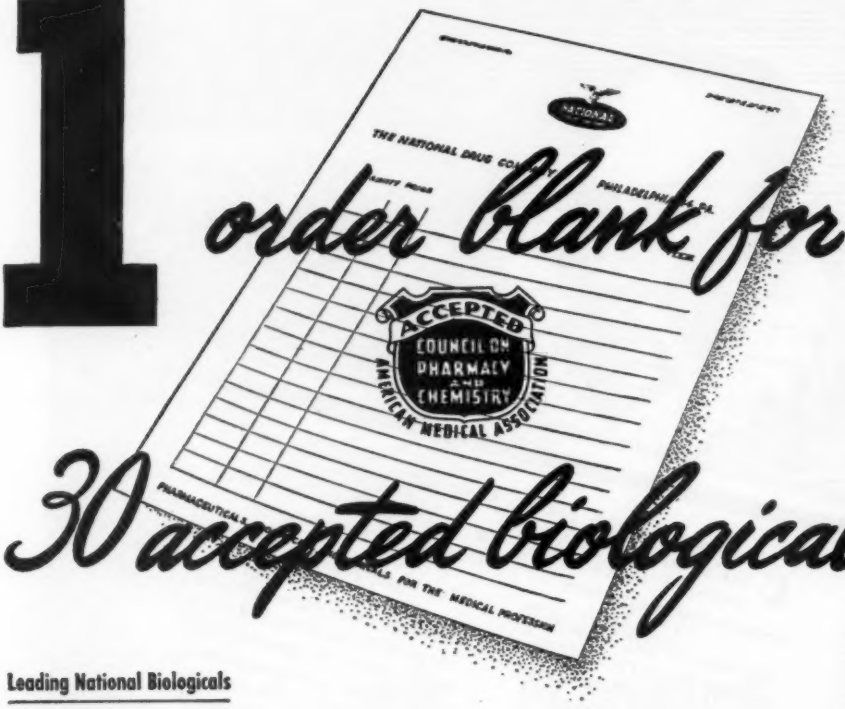
AS AN AID IN THE PREVENTION OF DENTAL CARIES

AYERST, McKENNA & HARRISON Limited

22 EAST 40TH STREET, NEW YORK 16, N. Y.

"... short sentences drawn from long experience"
Cervantes, Spanish poet, dramatist, and novelist, approved of "short sentences drawn from long experience."
The story of LIQUID PEPTONOIDS* WITH CREOSOTE can be told in such "short sentences drawn from long experience."
● For over fifty years physicians have continued to prescribe it.
● It helps arrest harassing cough.
● It promotes expectoration.
● It aids in checking extension of inflammatory processes.
● It is highly palatable.
Each fluid ounce contains 2 minims of pure beechwood creosote and 1 minim of guaiacol, combined with predigested beef, wheat, and milk. This combination increases palatability, lessens likelihood of gastric reaction.
LIQUID PEPTONOIDS
Reg. U. S. Pat. Off.
with CREOSOTE
SUPPLIED: Bottles containing 6 and 12 fl. ozs.
*The word PEPTONOIDS is a registered trademark of The Arlington Chemical Company.
LIQUID PEPTONOIDS
WITH CREOSOTE
THE ARLINGTON CHEMICAL COMPANY
YONKERS
NEW YORK

1 order blank for 30 accepted biologicals



Leading National Biologicals

Allergenic Extracts
Diphtheria & Tetanus Toxoids Combined (A.P.)
Diphtheria-Tetanus-Pertussis Combined Vaccine (A.P.)
Diphtheria Toxoid (A.P.)
Immune Globulin (Human)
Pertussis Vaccine (Double Strength)
Pertussis Vaccine (A.P.)
Scarlet Fever Streptococcus Toxin for Immunization
Staphylococcus Toxoid
Staphylococcus Toxoid-Vaccine Vatex
Staphylococcus Vaccine
Tetanus Toxoid (Alum Precipitated)
Typhoid Vaccine

The fact that thirty Council-Accepted biologicals could be placed on one order blank of The National Drug Company is a significant description of the policies of this well-known firm.

Old enough to have the stability of a conservative tradition; young enough in spirit to be excited by an enlarged and diversified program of medical research, The National Drug Company is dedicated to the principles guiding the American medical profession and its national associations.

NATIONAL DRUG COMPANY

THE NATIONAL DRUG COMPANY
PHILADELPHIA 44, PA.

PHARMACEUTICALS, BIOLOGICALS, BIOCHEMICALS FOR THE MEDICAL PROFESSION

DO YOUR DIABETIC PATIENTS COOPERATE FULLY?

A vital phase of diabetes management is the daily testing and recording of the patient's urine-sugar. At one time this involved such inconvenience, loss of time and technical difficulty as to lead to carelessness and lack of full cooperation by the patient. But these objections have been completely overcome with the introduction of—

CLINITEST

The Tablet, *No Heating* Method for Detection of Urine-Sugar

SIMPLE — SPEEDY — COMPACT — CONVENIENT

Clinitest is distributed through regular drug and medical supply channels.

Identification cards for the protection of your diabetic patients now available *free* upon request.

AMES COMPANY, Inc. • Elkhart, Indiana

Speed Recovery in

CERVICITIS

PENICILLIN VAGINAL SUPPOSITORIES

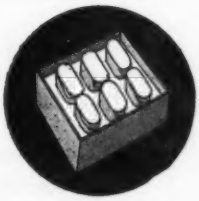
Schenley

Particularly useful in the medical and surgical management of cervicitis due to (or complicated by) penicillin-sensitive organisms.

ADVANTAGES • Potent dosage at site of infection—each suppository provides 100,000 units of penicillin • Painless administration • Simplicity and convenience.

Early favorable response establishes the effectiveness of Penicillin Vaginal Suppositories Schenley.

Suggested Dosage: One suppository on retiring or as required.



Supplied in boxes of 6 and 12

SCHENLEY LABORATORIES, INC.
Executive Offices: 350 Fifth Ave., New York 1, N. Y.

© Schenley Laboratories, Inc.

Illustration by Herman Giesen

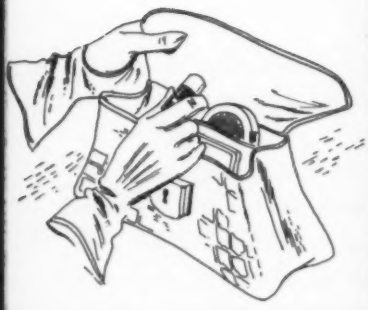
"The Bends"

PHYSICIANS are familiar with caisson disease, the industrial hazard encountered in construction of bridges, tunnels, and skyscrapers where workers breathe air under pressures of more than one atmosphere.

The first real advance in treatment and prevention of this interesting disorder came during the building of the New York Hudson tunnels under the North River in 1894. There the first decompression chamber was built and life became bearable to the "sand hog." Through ability to control and treat "the bends," medical science has made possible many of the major structural developments of the day.

Careful medical investigations, followed by the application of techniques based on the new facts, present a familiar pattern to physicians. The Lilly Research Laboratories collaborate with investigators in many fields of medicine on problems of mutual interest. The result of these efforts is reflected in the new and improved medication being made available for the physician's prescription.

FOR THE RELIEF OF NASAL CONGESTION



INHALER TUAMINE (2-Aminoheptane, Lilly) produces rapid, effective shrinkage of the nasal mucosa without disagreeable side-effects. Inhaler 'Tuamine' may be used as an effective adjunct to other therapy as well as to maintain vasoconstriction and drainage following office treatment.

For home use, Solution 'Tuamine Sulfate' (2-Aminoheptane Sulfate, Lilly), 1 percent, administered by spray or dropper produces prompt, prolonged vasoconstriction. There is no secondary engorgement or central-nervous-system stimulation.

Solution 'Tuamine Sulfate,' 2 percent, is recommended for office procedures in which maximum shrinkage is desired.

'Tuamine' preparations are stocked by all prescription drug stores.

ELI LILLY AND COMPANY

INDIANAPOLIS 6, INDIANA, U. S. A.

The so-called "Unknown Factors" and...

VITAMINS

Lederle

For many years, Lederle has led in the introduction of new vitamin combinations which have contained several of the so-called "unknown factors." These have included such substances as calcium pantothenate, pyridoxine (B_6), choline, inositol and folic acid. These factors have been "unknown" in the sense that while they were chemically recognizable and their effects in animals were clearly demonstrable, their precise usefulness in man had not been determined.

Recently, FOLVITE* Folic Acid has been shown to be the nutritional factor specific for red blood cell maturation in bone marrow. Thus, *Lederle* pioneering has been shown to have a sound basis in fact. It will continue to be our policy to give to physicians and their patients new vitamin factors, even though information upon them is not yet complete.

Malnutrition is present even in a rich and fast-moving economy. Vitamin deficiency is usually multivitamin deficiency and nutritional deficiency nearly always includes vitamin deficiency. Attention is drawn particularly to the following formulae—reinforced with FOLVITE Folic Acid which are widely used:

PERFOLIN Brand of Multivitamin Capsules**

Each capsule contains:

Vitamin A	25,000 U. S. P. Units
Vitamin D	1,000 U. S. P. Units
Thiamine HCl (B_1)	10 mg.
Riboflavin (B_2)	5 mg.
Niacinamide	150 mg.
Ascorbic Acid (C)	150 mg.
FOLVITE Folic Acid	5 mg.

FOLBESYN Parenteral Vitamins**

Each dose contains:

Vitamin B_1	10.0 mg.
Sodium Pantothenate	10.0 mg.
Niacinamide	50.0 mg.
Vitamin B_2	10.0 mg.
Vitamin B_6	5.0 mg.
Vitamin C	75.0 mg.
with diluent, containing FOLVITE Folic Acid	3.0 mg.

LEDERPLEX* Vitamin B Complex Tablets

Each tablet contains:

Thiamine HCl (B_1)	2.0 mg.
Riboflavin (B_2)	2.0 mg.
Niacinamide	10.0 mg.
Pyridoxine (B_6)	0.2 mg.
Calcium Pantothenate	3.0 mg.
Choline	20.0 mg.
Inositol	10.0 mg.
FOLVITE Folic Acid	0.2 mg.

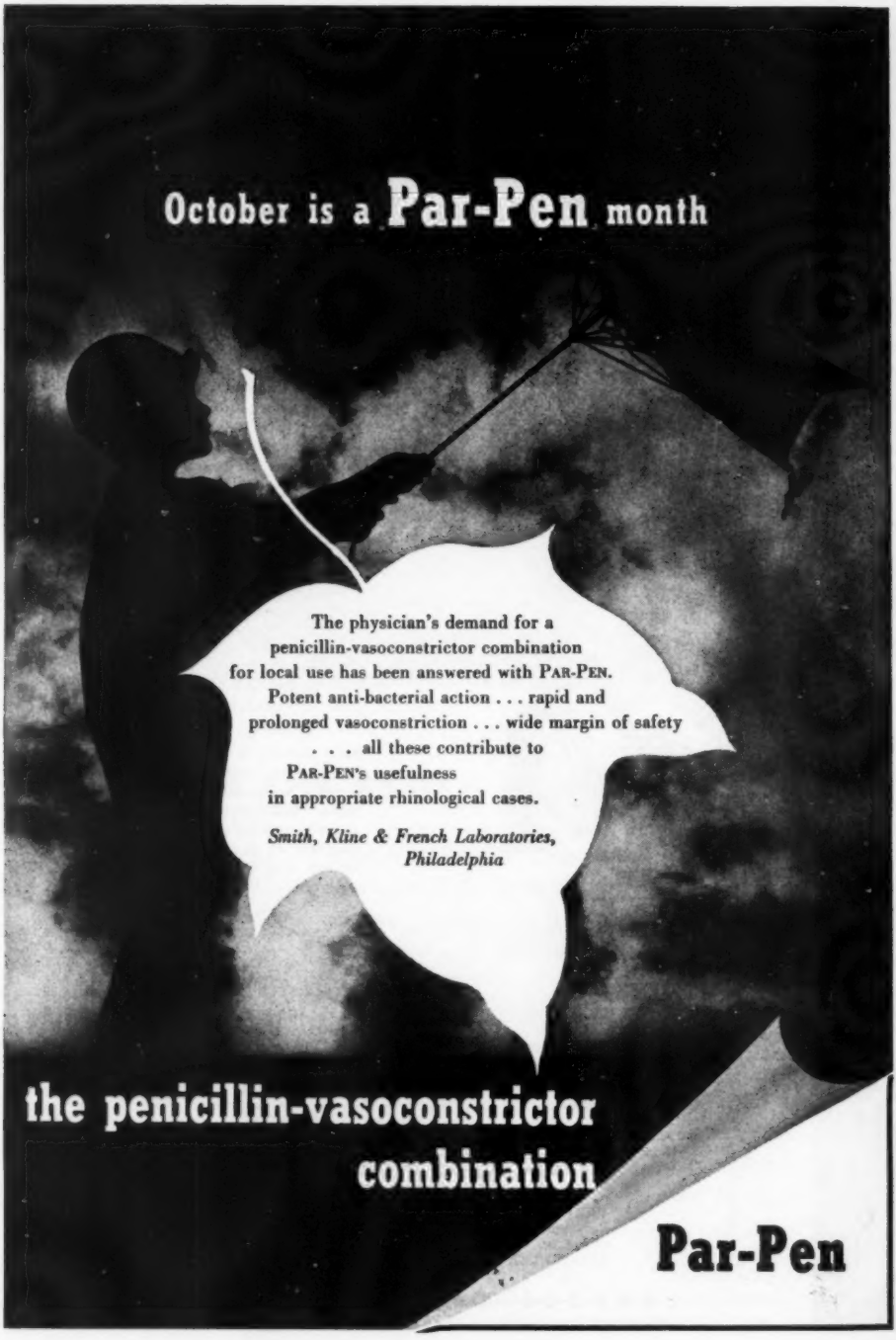
**Trade Mark*

***Reg. U. S. Pat. Off.*

PERFOLIN Multivitamin Capsules—*Bottles of 30 and 100.* FOLBESYN Parenteral Vitamins—*Single dose package contains 1 vial dried vitamins and 2 cc. ampul of diluent. Also in multiple package of 25 single doses.* LEDERPLEX Vitamin B Complex Tablets—*Bottles of 50, 100, 250, and 1000.*

LEDERLE LABORATORIES DIVISION

AMERICAN CYANAMID COMPANY • 30 ROCKEFELLER PLAZA, NEW YORK 20, N. Y.


October is a Par-Pen month
The physician's demand for a penicillin-vasoconstrictor combination for local use has been answered with PAR-PEN. Potent anti-bacterial action . . . rapid and prolonged vasoconstriction . . . wide margin of safety . . . all these contribute to PAR-PEN's usefulness in appropriate rhinological cases.
Smith, Kline & French Laboratories, Philadelphia
the penicillin-vasoconstrictor combination
Par-Pen

Amino-Concemin

a **synergistic** combination of
B Complex, Iron and **Amino Acids**

Specifically designed to shorten convalescence, through the catalytic action of amino acids on vitamin assimilation and iron utilization.[1, 2] Provides nutritional elements often deficient in the usual convalescent diet:

1. B COMPLEX—the established B vitamins, in high potencies, plus the entire B complex from three natural sources.
2. IRON—to counteract the frequently associated hypochromic anemia.
3. AMINO ACIDS—a 15% enzymatic yeast hydrolysate containing 10 essential amino acids with other amino acids and polypeptides, provides *extra* nitrogen as well as a synergistic effect on hemoglobin formation and vitamin utilization.

FORMULA

Each 45 cc. (average daily dose) contains:

Protein hydrolysate (45% amino acids)	6.75 Gm.
Thiamine hydrochloride	3.0 mg.
Riboflavin	2.0 mg.
Niacinamide	15.0 mg.
Pyridoxine hydrochloride	1.0 mg.
Peptonized iron, N.F.	0.4 Gm.
Liver, B complex fraction	0.5 Gm.
Rice bran extract	0.5 Gm.

Rich winey flavor

The delightful winey flavor of Amino-Concemin—unusual in a product containing amino acids, liver and iron—assures continued patient cooperation. Many find it particularly pleasant in milk or fruit juice. Dosage—15 cc. (1 tablespoon) three times a day, with or before meals.

1. Jacobson M.: N. Y. State J. Med. *45*:2079-2080 (1945).
2. Ruskin, S. L.: Am. J. Dig. Dis.: *13*:110-122 (1946).

AVAILABLE AT HOSPITAL AND PRESCRIPTION PHARMACIES IN PINTS AND GALLONS

Trademark "Amino-Concemin" Reg. U. S. Pat. Off.

MERRELL 1828

The Wm. S. Merrell Company, Cincinnati, U. S. A.

Penicillin by mouth

for adjunctive penicillin therapy

Bristol Penicillin Tablets provide an oral dosage form most useful in the withdrawal period when injection therapy has controlled the more acute stages of an infection and relapse is to be avoided. They are also employed for prophylaxis in tonsillectomy and tooth extraction. Therapeutic levels may be maintained by administering approximately five times the intramuscular dose.

Bristol Penicillin Tablets are available in bottles of 12, each scored tablet containing 100,000 units. They are compounded of crystalline sodium penicillin G buffered with calcium carbonate, and are available for your prescription through your pharmacist.

No refrigeration required.

Bristol

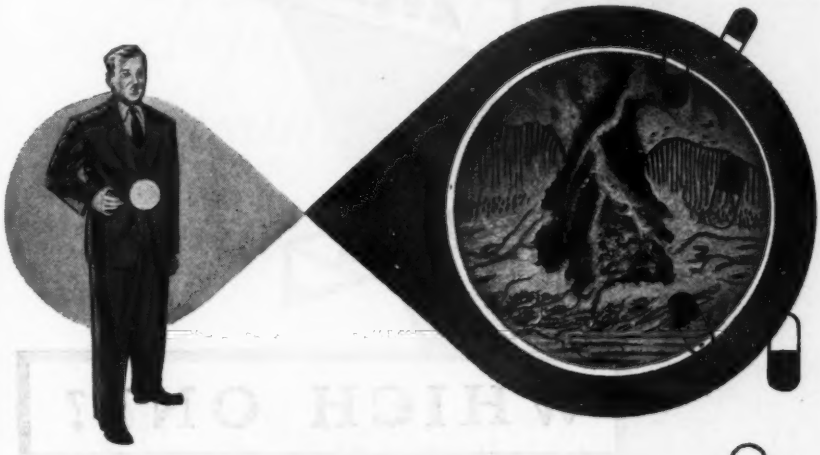
LABORATORIES INC. SYRACUSE, NEW YORK

ANNOUNCING:

prompt and sustained relief in
GASTRIC and DUODENAL ULCER

PEPSIN INACTIVATION BY ADSORPTION

NEW NONCONSTIPATING antacid WITHOUT BY-EFFECTS



RESINAT approaches the ideal in an antacid preparation. This fact has been established by extensive clinical investigation.

Unlike all other antacids, RESINAT is an inert and insoluble substance that cannot enter into chemical reaction with stomach contents nor be absorbed into the system. This means that RESINAT, in spite of its great acid normalizing power, does not disturb the acid-base balance of body fluids; that it inactivates pepsin by adsorption and normalizes the acidity of the gastric juice without causing "rebound" or alkalinization. Then, too, RESINAT spares the patient annoying side-effects commonly associated with antacid therapy—constipation, diarrhea or eructation.

RESINAT is effective in the treatment of peptic and duodenal ulcers, gastritis and hyperacidity.

DOSAGE: one or two capsules (0.25 Gm. each) as needed for relief. Supplied in bottles of 50, 100, 500 and 1,000.

a research product of

THE NATIONAL DRUG COMPANY
PHILADELPHIA 44 • PENNSYLVANIA

RESINAT
RESIN ANTACID

PHARMACEUTICALS, BIOLOGICALS, BIOCHEMICALS FOR THE MEDICAL PROFESSION

STREET
AVENUE
Place
Road
Boulevard
WHICH ONE?
Remembering multiple names is no longer a problem when it comes to ordering the male sex hormone for parenteral use. Merely specify the name under which it has been accepted for inclusion in N.N.R.
TESTOSTERONE PROPIONATE "RARE CHEMICALS"
The Only Council Accepted Androgenic Preparation
Supplied in 1 cc. ampules, 5, 10 and 25 mg., in boxes of 3, 6 and 50; also 10 cc. vials, 25 mg. per cc., and 6 cc. vials, 50 mg. per cc.
Now available at
materially reduced prices
RARE CHEMICALS, INC., Harrison, N. J.
West Coast Distributors: GALEN COMPANY, Richmond, Calif.
114J

Uniformity

Dependability in digitalization and maintenance

Sensible economy

Pil. Digitalis (*Davies, Rose*)

0.1 Gram (1½ grains)

Physiologically Standardized

Each pill contains 0.1 Gm. (1½ grs.) Powdered Digitalis, produced from carefully selected leaf of Digitalis purpurea, therefore of an activity equivalent to 1 U.S.P. XII Digitalis Unit.

When Pil. Digitalis (*Davies, Rose*) are dispensed on a prescription, the physician is assured that the patient receives digitalis in its completeness and obtains the full benefit of the therapy.

Trial package and literature sent to physicians on request.

Davies, Rose & Company, Limited

Manufacturing Chemists, Boston 18, Massachusetts

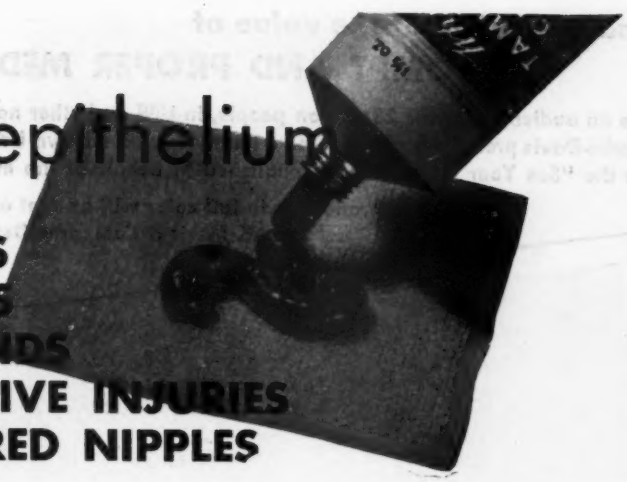
D81

Swift regeneration in

Severe 2nd and 3rd degree burn, treated with pressure gauze dressing of White's Vitamin A and D Ointment. Immediate relief of discomfort.

Same patient 3 months later (treatment was discontinued after one month). Practically complete re-epithelization without resort to skin-grafting.

White's



healing epithelium

in BURNS
ULCERS
WOUNDS
AVULSIVE INJURIES
FISSURED NIPPLES

Advantages of White's Vitamin A and D Ointment:

... hastens healthy granulation and epithelization
... destroys no epithelial elements
... inhibits infection
... does not produce contractures

White's Vitamin A and D Ointment provides the natural vitamins A and D, derived from fish liver oils, in the same ratio as found in cod liver oil, in a lanolin-petrolatum base. Pleasantly fragrant; keeps indefinitely at ordinary temperatures; does not stain tissues. In 1.5 oz. tubes; 8 oz. and 16 oz. jars; 5 lb. containers.

Vita A & D Ointment

WHITE LABORATORIES, INC., Pharmaceutical Manufacturers, Newark 7, N. J.

Reminding people of the value of
PROMPT AND PROPER MEDICAL CARE

To an audience of over 23 million people, in LIFE and other national magazines, Parke-Davis presents a message on a timely subject (shown below). It is No. 207 in the "See Your Doctor" series published in behalf of the medical profession.

A reproduction in full color will be sent on request. Write to Parke, Davis & Company, Detroit 32, Michigan.

Some things you should know about sleeping pills
No. 207 in a series of messages from Parke, Davis & Co. on the importance of prompt and proper medical care.
Used wisely, under the guidance of a physician, sleep-inducing drugs are one of modern medical science's important aids.
In many cases marked by a temporary anxiety, nervousness or physical discomfort, your doctor relies on them to supply the sleep or relaxation so vital to proper treatment.
Before an operation, these sleep-inducing drugs are often used to save the patient from a wakeful night of apprehension. These drugs are also used to prevent toxic reactions to local anesthesia, to inhibit convulsions, to make the pain-deadening action of other drugs more effective.
Many types of sleep-inducing drugs have been developed. Your doctor chooses among them according to the individual case.
Sleep-inducing drugs can be of great value. Like any beneficial product these drugs can be abused. Taken without your doctor's express orders, they may be dangerous. You have probably seen newspaper accounts of deaths or serious poisoning caused by excessive misuse of these drugs.
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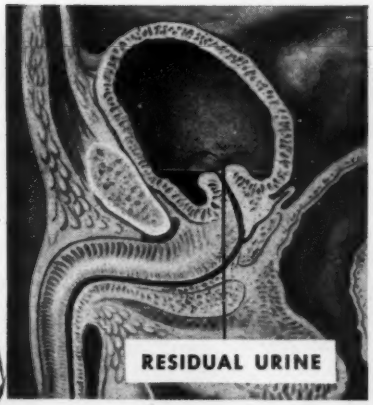

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when urinary stasis invites infection

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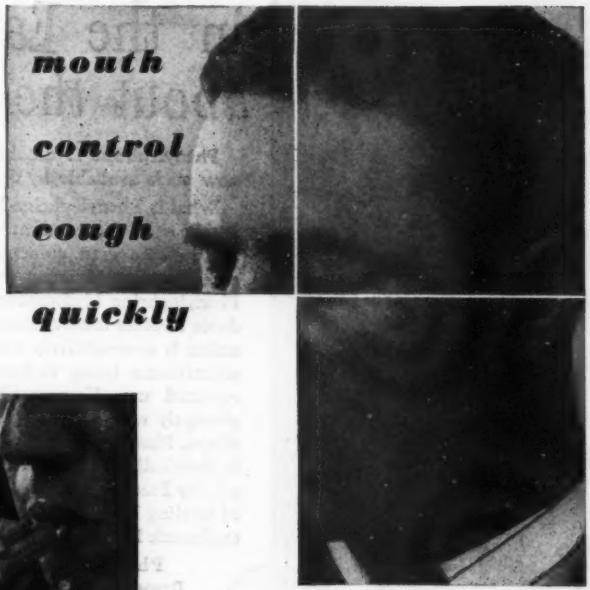

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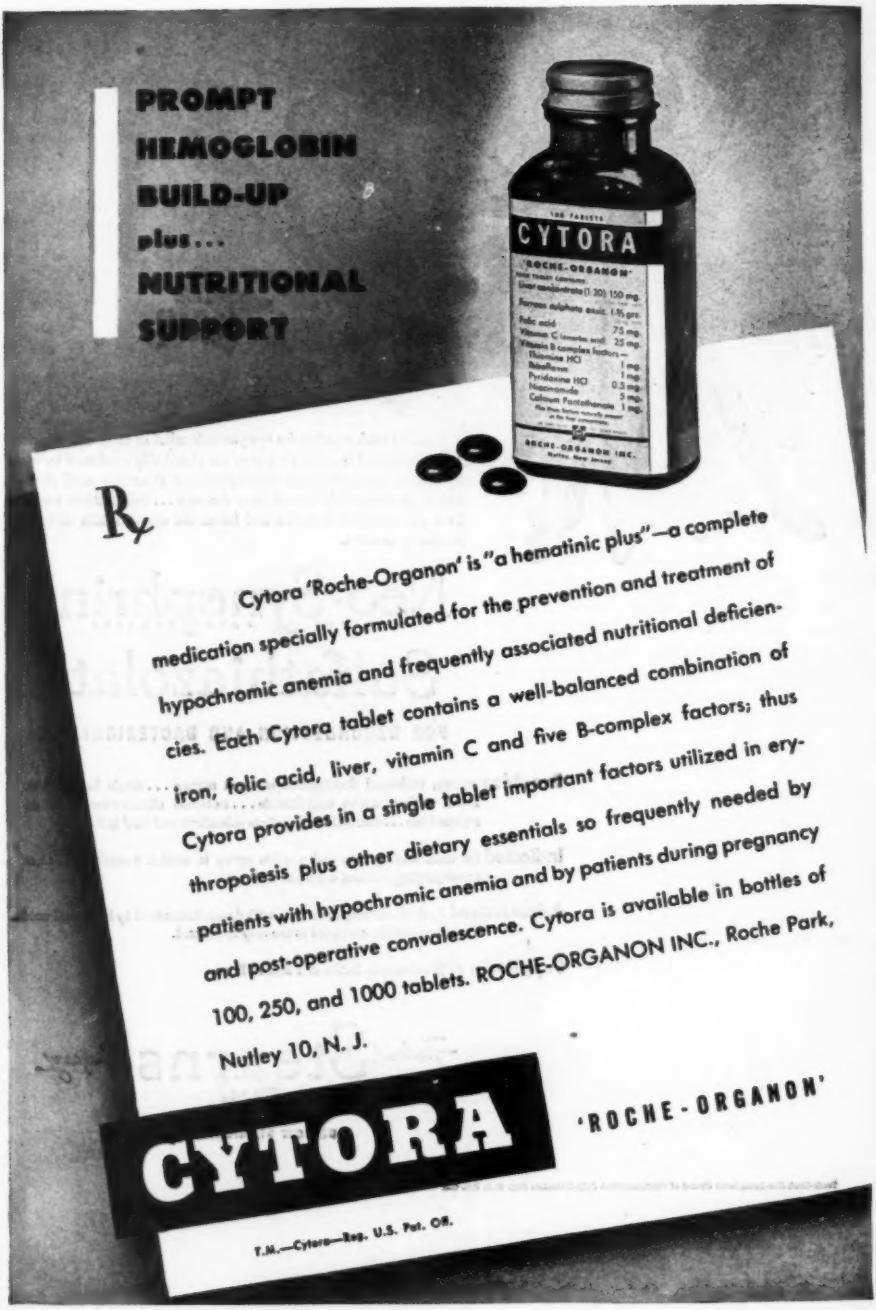
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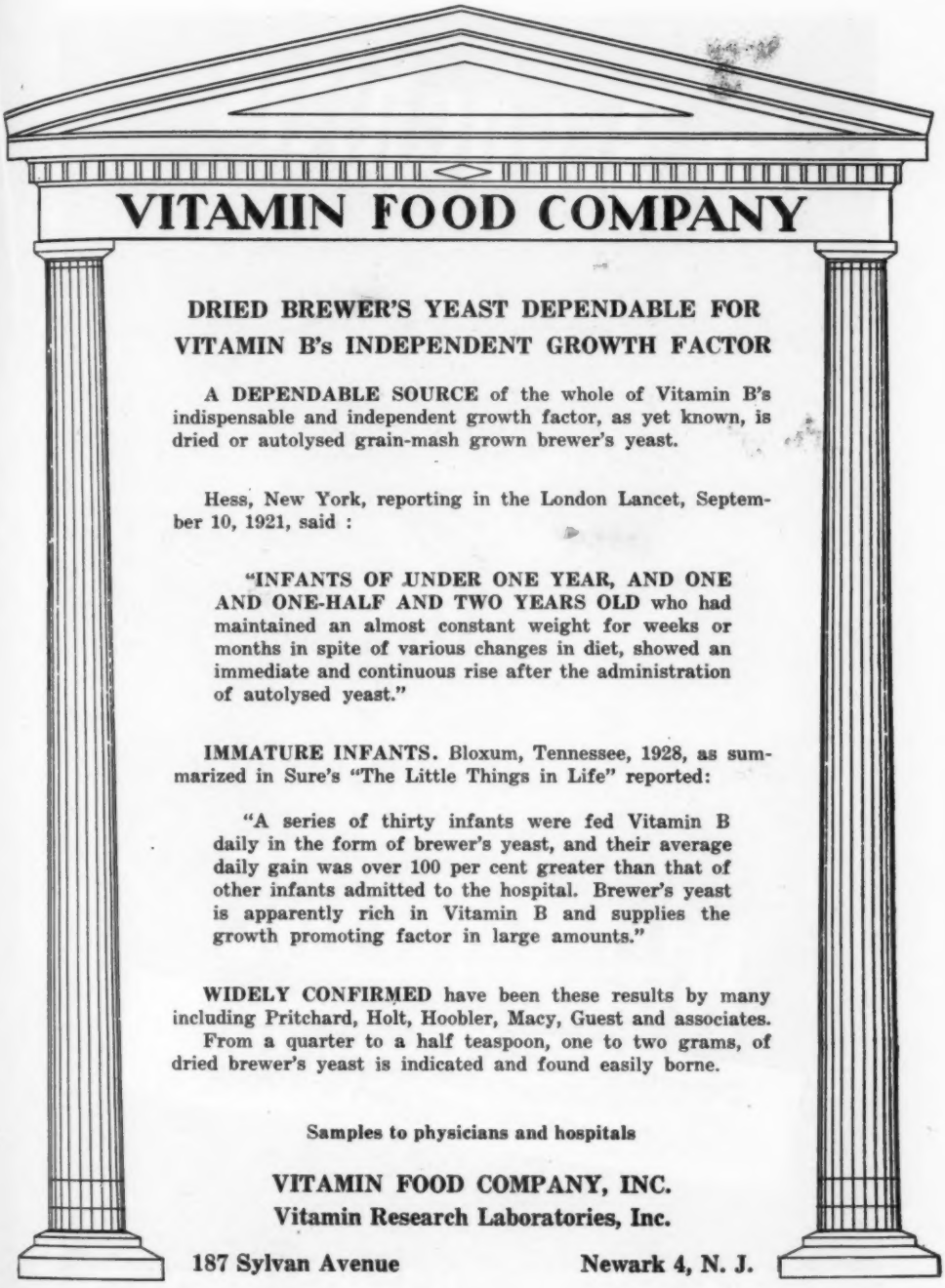

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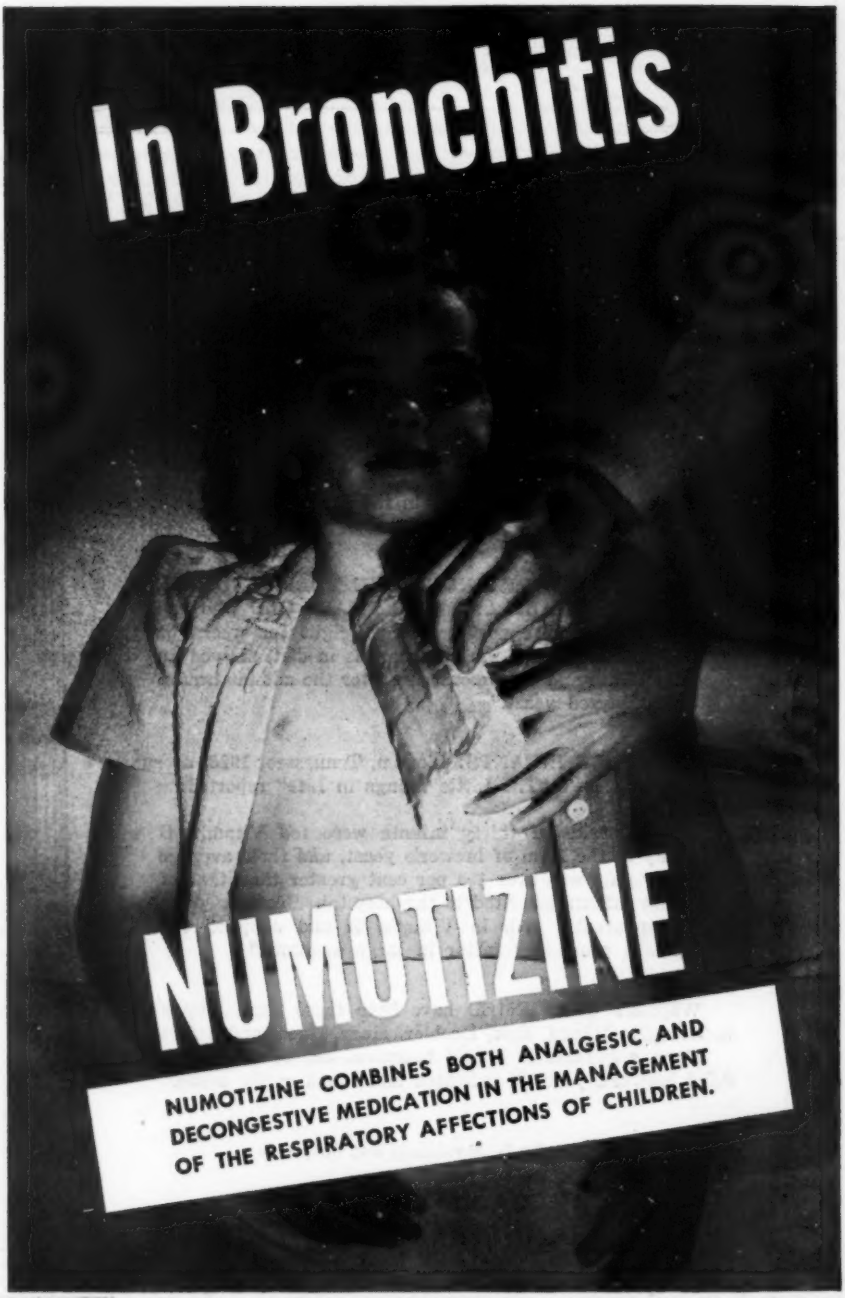
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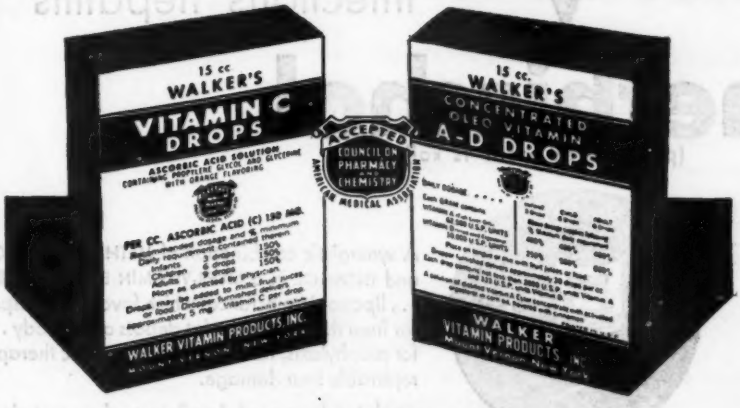

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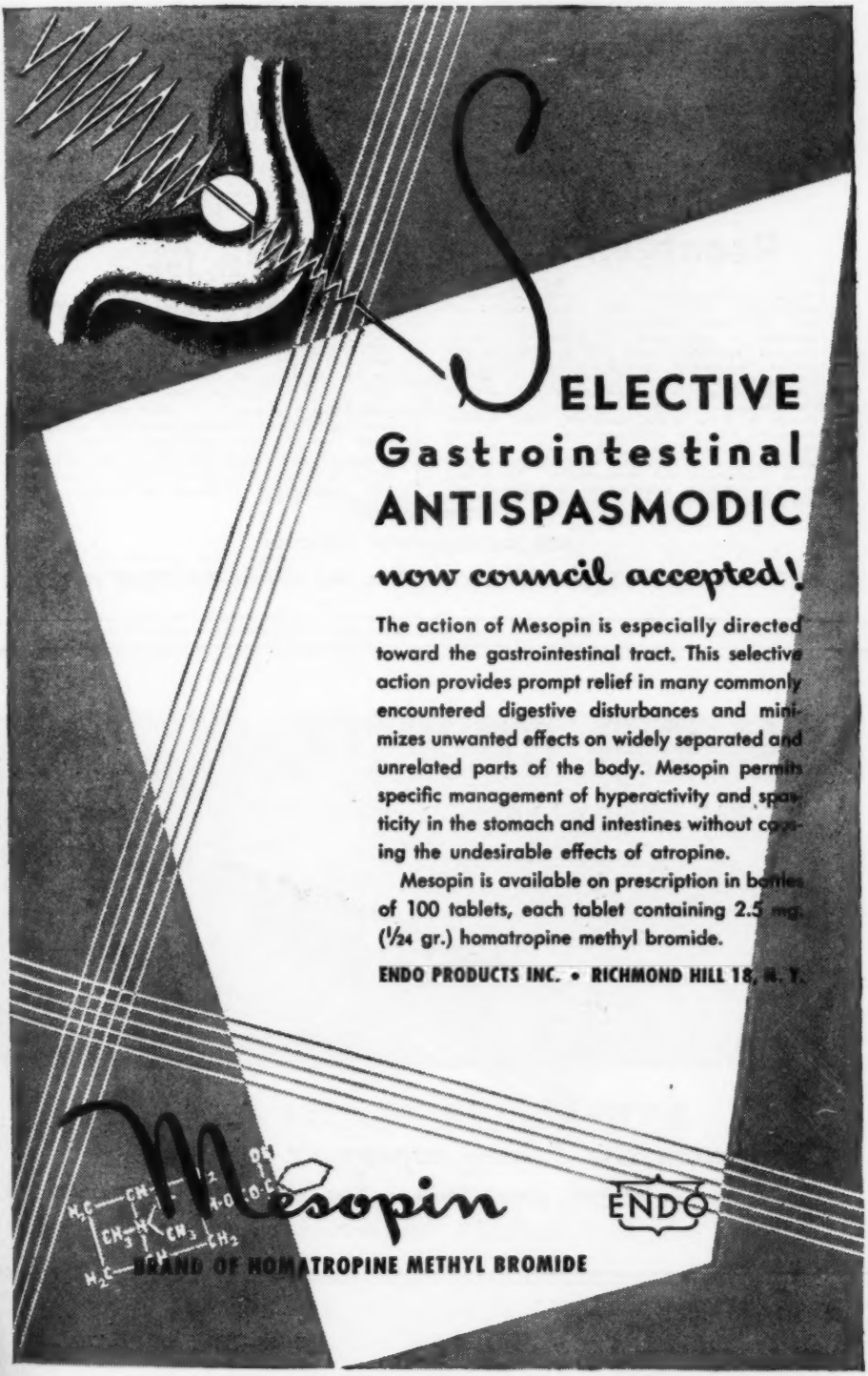
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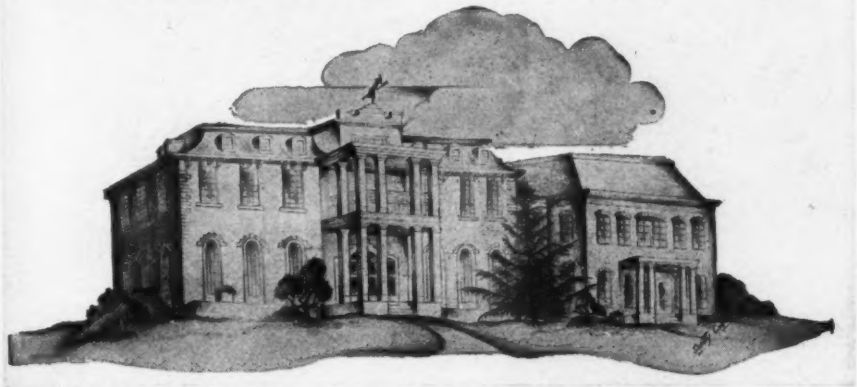

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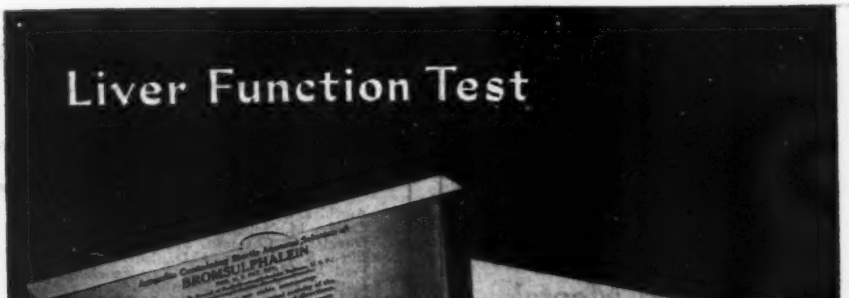

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Volume 40 OCTOBER 1947 Number 10

THE TREATMENT OF ROCKY MOUNTAIN SPOTTED FEVER WITH PARA-AMINO-BENZOIC ACID: A COMPREHENSIVE PLAN*

By SAMUEL F. RAVENEL, M.D.
Greensboro, North Carolina

The term "Rocky Mountain spotted fever" is obviously a geographical misnomer since this disease has been reported in 47 of the 48 states. A decade ago 70 per cent of the cases occurred in the Mountain and Pacific states, while last year 87 per cent were reported from the Atlantic and Central states. This change in the geography of the disease is probably due to (a) better recognition and reporting of cases east of the Rockies; (b) a reduction in the number of cases in the West as a result of population shifts from infected areas, preventive vaccination, and educational measures; and (c), in my opinion, an increase in the number of cases in the South Atlantic states.

The conquest of acute infections has been so spectacular since the introduction of the sulfa drugs and the newer antibiotics that spotted fever has now become "Captain of the Men of Death" so far as infectious diseases are concerned. Were poliomyelitis to kill 18 patients out of 57 in one year in North Carolina, mass hysteria would result; when spotted fever did this in 1945 no one became excited. The situation in Maryland and Virginia is quite comparable. I submit and contend that from the standpoint of morbidity and mortality, spotted fever is a matter of extreme public health importance in our section.

In the early days the treatment of this very serious and often fatal disease was largely symptomatic. This simply enabled the patient to die or recover somewhat more comfortably. Unfortunately, the pathologic changes in the vascular system were so striking and so emphasized in pioneer studies that the dictum was laid down that parenteral administration of fluids was hazardous. As recently as 1943, Topping[1] wrote:

> ". . . an occasional patient will require an additional amount (of fluids) parenterally. This had perhaps better be given by hypodermoclysis rather than intravenously as there is some clinical evidence that any intravenous therapy is contraindicated." Martin[2] concluded that "blood transfusions probably also are contraindicated because of the endarteritis . . . However, if the anemia becomes marked, transfusions may be necessary."

For years those of us who were forced to battle with this fearful disease each summer were accustomed to administer intravenous fluids and blood transfusions with great freedom and apparently with considerable success. The rationale of these measures was arrived at empirically and as a result of long experience. It seemed to us that these patients should be and were benefited by measures calculated to prevent and overcome the phenomena of dehydration, depletion, anemia and metabolic starvation which appeared regularly in this severe disease. Such clinical "battles" sometimes were waged for a month or more and many desperately ill patients recovered, but our mortality over a period of years averaged about 25 per cent.

It was not until 1944 that the careful studies of Harrell, Venning and Wolff[3] revealed the pathologic physiology of Rocky Mountain spotted fever and explained why properly chosen intravenous supportive therapy was beneficial. They showed that because of the widespread vascular lesions plus starvation there was a tremendous loss of circulating body fluids and

*Read in Section on Pediatrics, Southern Medical Association, Fortieth Annual Meeting, Miami, Florida, November 4-7, 1946.

*From the Pediatric Service of St. Leo's Hospital and the Sternberger Children's Hospital.

protein, with lowering of blood chlorides, elevation of blood nonprotein nitrogen and potential or actual development of peripheral circulatory collapse. They suggested that supportive therapy should include adequate amounts of plasma and whole blood in addition to glucose, salts, vitamins and amino acids and should be controlled by careful laboratory studies. Furthermore, they pointed out that because of the intranuclear location of rickettsia in this disease any therapeutic agent must pass through two cell membranes in order to reach the organisms. This explains, in the opinion of these authors, why Topping's immune rabbit serum[1] appears to be effective only in the first three days of the rash before many parasites have become established in cells. Unfortunately, most patients with spotted fever come under treatment much later than this.

The sulfonamides are not only useless but probably harmful in this disease. Experimentally, sulfonamide treated guinea pigs died sooner than the untreated controls.[4] Since the sulfonamides and para-aminobenzoic acid are antagonistic in action, use of the former is contraindicated in patients treated with para-aminobenzoic acid.

Although rickettsia are reported to be sensitive to penicillin, this has proved useless in treating spotted fever.

The experimental and clinical background for the use of para-aminobenzoic acid in the treatment of spotted fever dates from 1942. Snyder, Maier and Anderson[5] showed that its oral administration would reduce the mortality of experimental murine typhus in white mice, while Hamilton, Plotz and Smadel[6] found that it would inhibit the growth of both epidemic and murine typhus rickettsia in chick embryos. These investigators and others[12 13] feel that para-aminobenzoic acid interferes in some way with their proliferation within tissue cells, probably by stimulation of cellular metabolism. This inhibits the infecting organisms sufficiently to permit development of a lasting immunity. This hypothesis also explains why para-aminobenzoic acid may be therapeutically effective even late in the course of Rocky Mountain spotted fever when the rickettsias have become not only intracellular but also intranuclear.

Yeomans, Snyder, Murray, Zarafonetis and Ecke[7] treated twenty cases of louse borne human typhus with para-aminobenzoic acid with forty-four untreated patients as controls. They felt that the course of the disease was favorably modified if the patient were treated in the first week of illness. (In the light of present knowledge both dosage and blood concentration of the drug were probably too low.)

Anigstein and Bader[8] found para-aminobenzoic acid effective therapeutically in guinea pigs infected with Rocky Mountain spotted fever rickettsia. All the control animals died, while those fed 2 per cent para-aminobenzoic acid in the diet escaped infection or recovered. Hamilton[9] reported that para-aminobenzoic acid inhibits the growth of spotted fever rickettsia in chick embryos to an even greater extent than typhus rickettsia. Rose, Duane and Fischel[10] treated a 46-year-old woman suffering from moderately severe spotted fever with para-aminobenzoic acid. She recovered with great rapidity. Maroney and Davis[11] reported the dramatic recovery of a 3-year-old child in whose case treatment with para-aminobenzoic acid was begun on the twelfth day of severe spotted fever.

Murray, Zarafonetis and Snyder[12] found that para-aminobenzoic acid protected 100 per cent of gerbils (small South African rodents) from multi-lethal doses of Rickettsia orientalis, the causative organism of tsutsugamushi disease (scrub typhus). Tierney[14] treated 18 cases of severe human tsutsugamushi disease with large doses of para-aminobenzoic acid. Blood levels of 30 to 60 milligrams per cent were maintained. He concluded that para-aminobenzoic acid is an effective therapeutic agent in this disease.

Smith[15] reported 29 patients with endemic typhus treated with moderate doses of para-aminobenzoic acid. He felt that they recovered more rapidly than untreated control cases. (It is probable that better results would have been achieved with larger doses.)

REPORT OF CASES

Case 1, Chart 1.—B. R., a white boy aged 17 years, entered St. Leo's Hospital June 4, 1946, with a history of tick bite 11 days, headache and malaise 8 days, fever and chills 7 days, rash 6 days and delirium 2 days before admission.

Physical Examination.—Examination revealed a delirious, dehydrated boy with the classic hemorrhagic rash of spotted fever, conjunctivitis, palatal enanthema, slight scrotal edema. Laboratory examination revealed a hemoglobin level of 13 grams, 4 million erythrocytes, 10,600 leukocytes with 76 per cent neutrophils, a negative urinalysis. The flocculation test for syphilis was negative, as was the Widal reaction and agglutination against Proteus OX19. The serum protein was 6.6 grams per 100 c. c.

Treatment.—An adequate fluid intake was maintained by the oral route supplemented by intravenous injections. Vitamin B complex and ascorbic acid were given intramuscularly. Four grams of sodium chloride were included in the daily diet. Plasma and blood were given on several occasions. Para-aminobenzoic acid 2.5 grams in 25 c. c. of 5 per cent sodium bicarbonate solution was given by mouth every 2 hours for the first two days. The blood level of para-aminobenzoic acid was only 4 mg. per 100 c. c. at the end of this time. Accordingly, the drug was increased to 5 grams every 2 hours in 50 c. c. of sodium bicarbonate solution. In 24 hours the blood level was 18 mg. and a day later 32 mg. per 100 c. c. The temperature dropped sharply on the fifth day, reached normal on the sixth day and remained there. The rash faded with great rapidity on the sixth day, the sensorium cleared over night, and the boy was practically well. The Weil-Felix agglutination test with Proteus OX19 was positive 1:2560 on June 16, and the complement fixation reaction positive for Rocky Mountain spotted fever 1:256 on June 12.

Judging from experience with spotted fever in the past, this was a brilliant and spectacular therapeutic result in a rather severe case. Ordinarily this boy might have been expected to be extremely sick for two or three weeks. Charts of extremely severe and moderately severe cases treated prior to para-aminobenzoic acid are shown by way of contrast (*Charts 2* and *3*).

Case 2, Chart 4.*—P. M., a white girl aged 4 years, was admitted to the Sternberger Children's Hospital, July 24, 1946, with a history of tick bite, high fever and chills for 7 days, rash and delirium for 4 days.

Physical Examination.—She appeared to be quite ill, was delirious, dehydrated, incoordinate and breathed rapidly and deeply. The pulse rate was 148 and blood pressure 82/60. There was a generalized hemorrhagic macular rash most intense on face, buttocks and extremities, and a palatal enanthema. The spinal fluid was normal chemically and cytologically. The carbon

*This case is reported through the courtesy of Dr. Roy M. Smith, Greensboro, N. C.

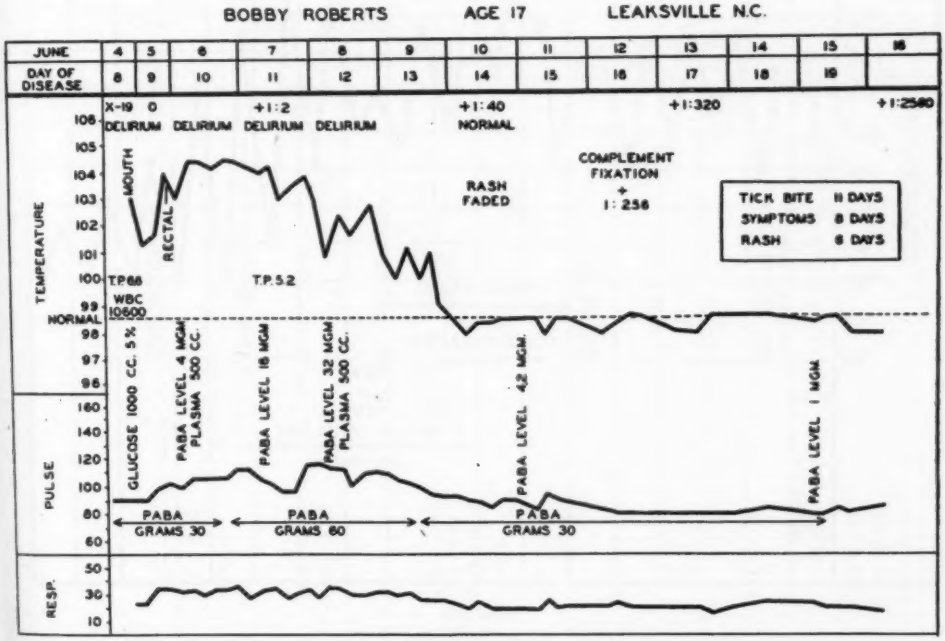

Chart 1, Case 1
Para-aminobenzoic acid (PABA) therapy in severe case of Rocky Mountain spotted fever.

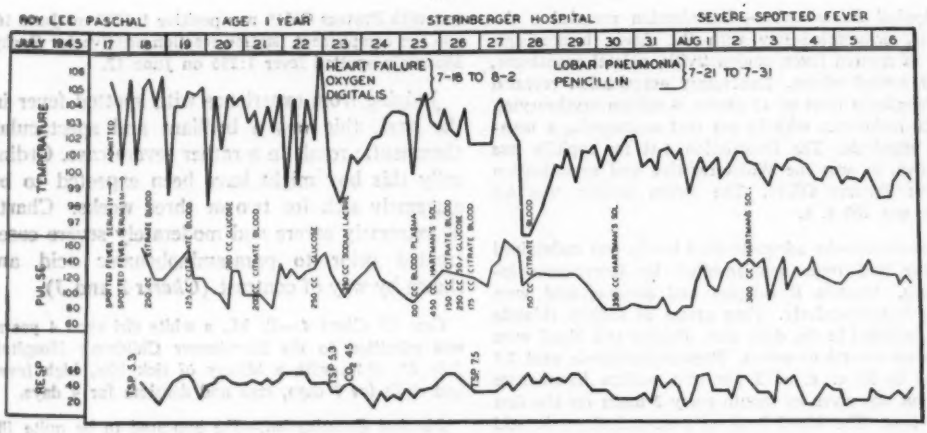

Chart 2
Extremely severe case treated before PABA era.

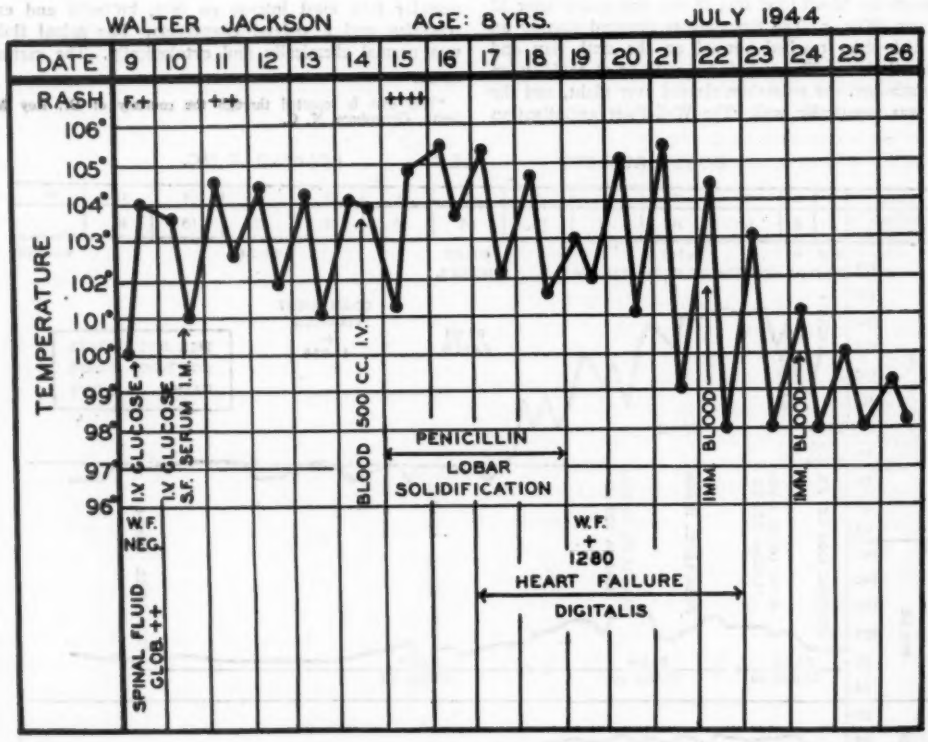

Chart 3
Moderately severe case, before PABA era.

dioxide combining power of the blood was 32 volumes per cent, serum protein level 5.9 grams per 100 c. c., Widal reaction and agglutination against Proteus OX19 negative.

Treatment.—Dehydration and acidosis were rapidly overcome with sixth molar sodium lactate and glucose in lactate-ringer's solution parenterally. She was given 3 grams of para-aminobenzoic acid every 2 hours by mouth (1 gram per pound per 24 hours) and adrenal cortical extract, vitamins B complex, C and K parenterally. Plasma and blood were administered at appropriate intervals. Defervescence began the third day and was complete the fourth. The rash faded with great rapidity after the fourth day in striking contrast to its usual course in severe spotted fever. Ordinarily the rash becomes progressively more intense, widespread, and hemorrhagic for at least two weeks.

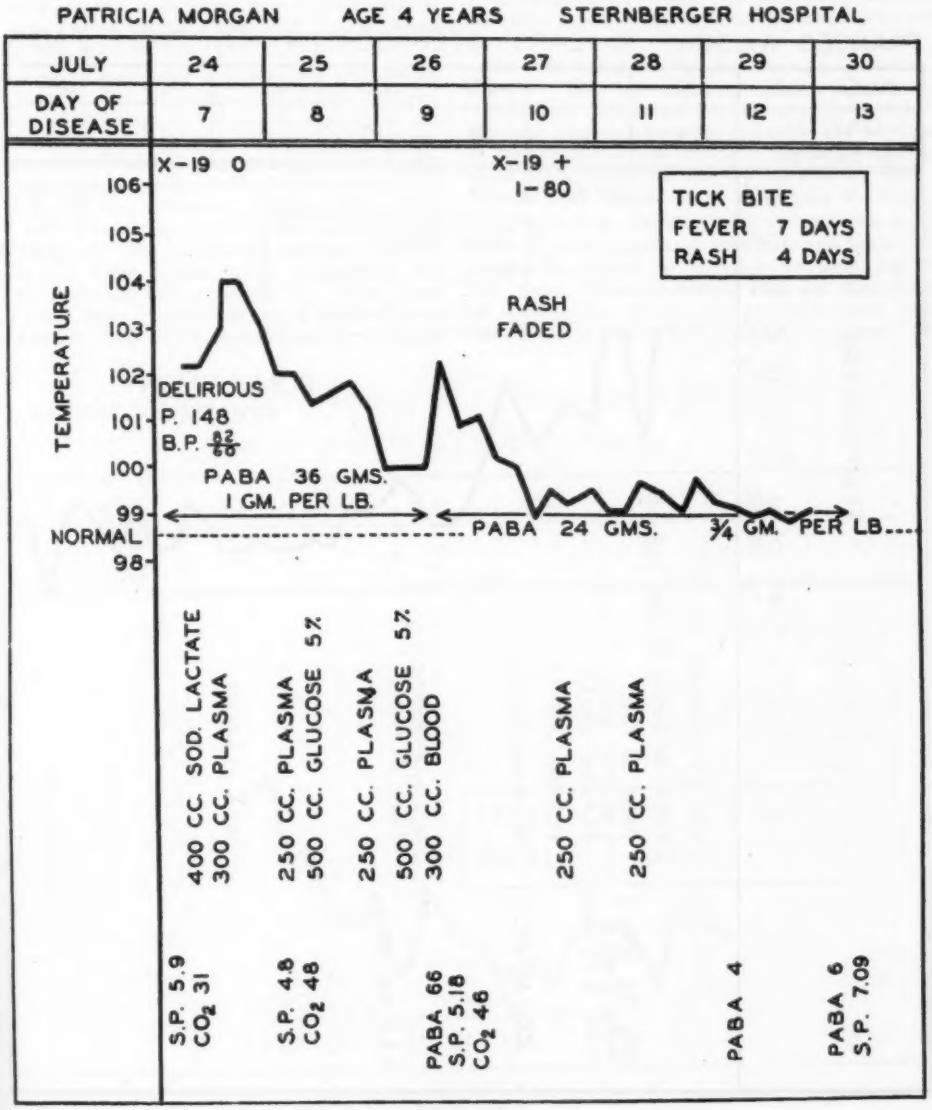

Chart 4, Case 2
PABA therapy, severe case, excellent result.

This also may be described as a brilliant therapeutic triumph in a very sick child whose febrile fastigium in the pre-para-aminobenzoic acid era would probably have exceeded two weeks in duration. It is worthy of note that this patient was already in acidosis on admission and that without adequate laboratory control this factor alone might have become extremely serious. The blood level of para-aminobenzoic acid was 66 milligrams per cent on the third day and 54 on the fourth after the dose was decreased to 2 grams every two hours.

Case 3, Chart 5.—F. W., a white girl of 10 years, entered the Sternberger Children's Hospital, August 10,

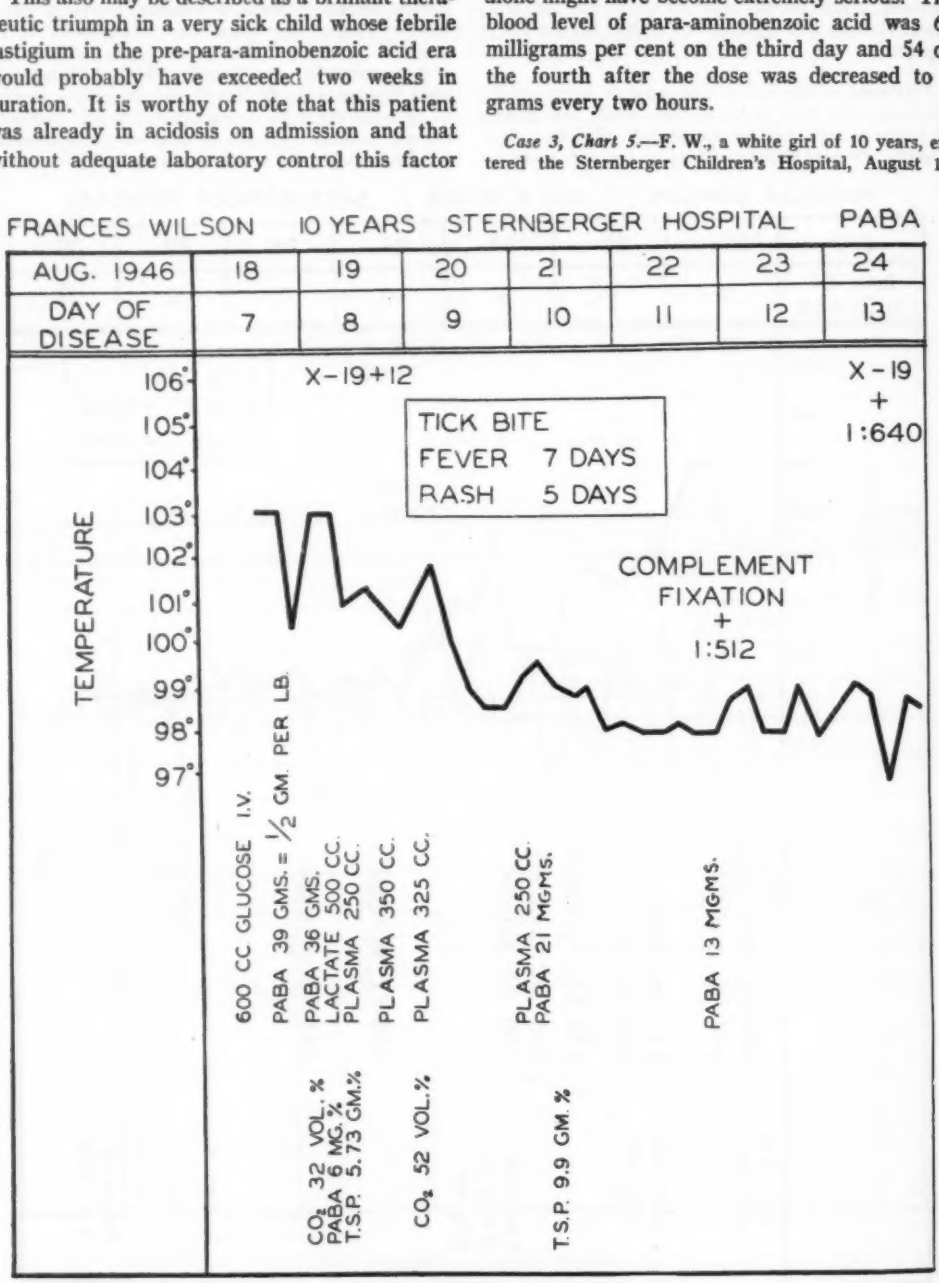

Chart 5, Case 3
Excellent result with para-aminobenzoic acid therapy.

1946, with a history of tick bite two weeks, headache, chills, high fever, and backache seven days, rash and inconstant delirium five days before admission.

Positive findings were: dehydration, the typical hemorrhagic rash of spotted fever involving the entire body, but with maximum intensity on extremities, conjunctivitis, strawberry tongue, moderate edema, positive Brudzinski and Kernig's signs, a rapid pulse. The spinal fluid yielded normal cytological and chemical findings and urinalysis and blood count were also negative, as was agglutination against Proteus OX19. The serum protein level was 5.76 grams per 100 c. c.

Intravenous glucose in lactate-ringer's and plasma were given in adequate amounts, and a high intake of vitamins A, B complex, C, D and K maintained. Six grams of para-aminobenzoic acid were given on admission and then 3 grams every two hours, buffered with 10 c. c. of chilled 5 per cent sodium bicarbonate solution per gram. The carbon dioxide combining power of the blood was 32 volumes per cent on the second day and 52 on the third. The temperature dropped to normal and the rash began to fade rapidly on the third day. She was practically well at the end of a week. There was a weight loss of 6 pounds in 6 days, obviously from loss of edema fluid. Blood obtained on the ninth day agglutinated Proteus OX19 1:320 and gave a positive complement fixation for spotted fever 1:512.

This appeared to be a brilliant therapeutic triumph in a moderately severe case of the disease.

Case 4, Chart 6.—L. S., a white girl aged 3, was admitted to the Sternberger Children's Hospital, August 9, 1946, complaining of fever (102°-104°) and chills for four days, a rash for three days, and vomiting for one day.

The child looked sick but was conscious and not dehydrated. There was a generalized pink macular and papular rash most intense on the extremities and buttocks and present on the palms and soles. The remainder of the examination was essentially negative. Urinalysis, blood count, Widal reaction and agglutination against Proteus OX19 revealed no deviation from the normal.

She was given adequate fluids and vitamins and 3 grams of para-aminobenzoic acid every two hours. The temperature dropped to normal in 24 hours, and the rash faded. Para-aminobenzoic acid was discontinued on the fifth day. On that day her blood serum agglutinated proteus OX19 1:640 and the complement fixa-

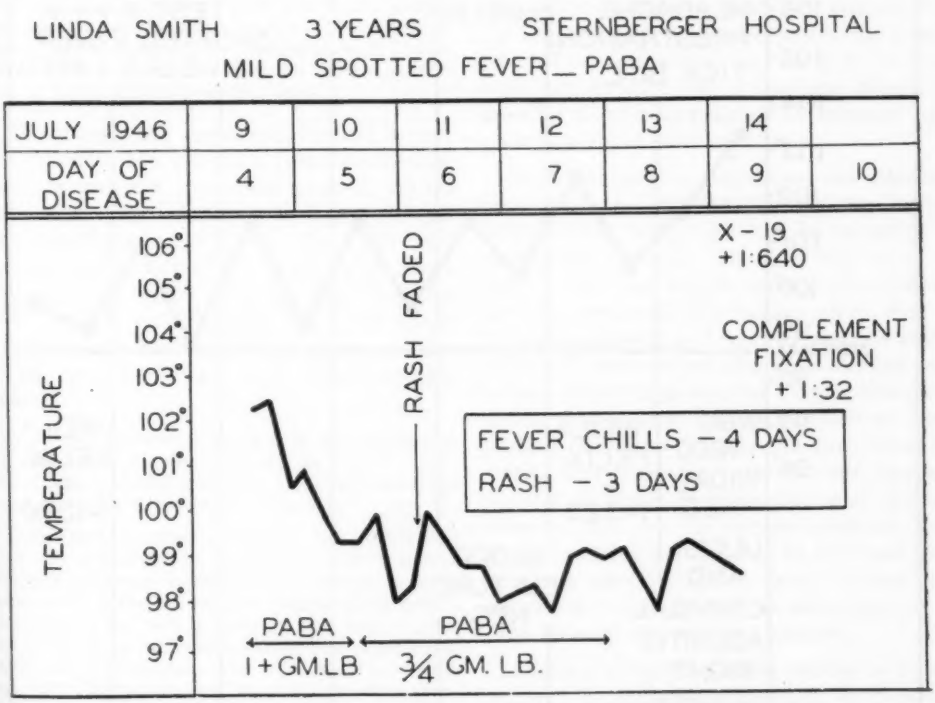

Chart 6, Case 4
Mild case of Rocky Mountain spotted fever with para-aminobenzoic acid therapy.

tion test for Rocky Mountain spotted fever was positive 1:32.

This was a mild case of spotted fever which, however, under treatment with para-aminobenzoic acid terminated with astonishing speed. By way of contrast the chart is shown (*Chart 7*) of a boy (before para-aminobenzoic acid) with spotted fever so mild that he had no trace of rash. Defervescence was not complete until the fourteenth day of the disease.

Case 5.—F. W., a white girl, aged 5 years, entered the Sternberger Children's Hospital, June 26, 1946, with a history of tick bite 10 days, high fever and chills six days, rash 4 days, vomiting and delirium 2 days before.

The child appeared to be very ill, was dehydrated and delirious. There was a fine hemorrhagic rash all over the body, most intense on face and extremities, present on palms and soles. Conjunctivitis, a coated tongue and a pulse rate of 160 were noted. The heart and liver were not enlarged.

Glucose in lactate-ringer's was given intravenously, vitamins A, B complex, C, D and K furnished in large amounts and para-aminobenzoic acid 2 grams per pound (5 grams every 2 hours in 40 c. c. of 5 per cent sodium bicarbonate solution) prescribed. After 12 hours there was considerable abdominal distension which was erroneously attributed to the sodium bicarbonate. Accordingly,

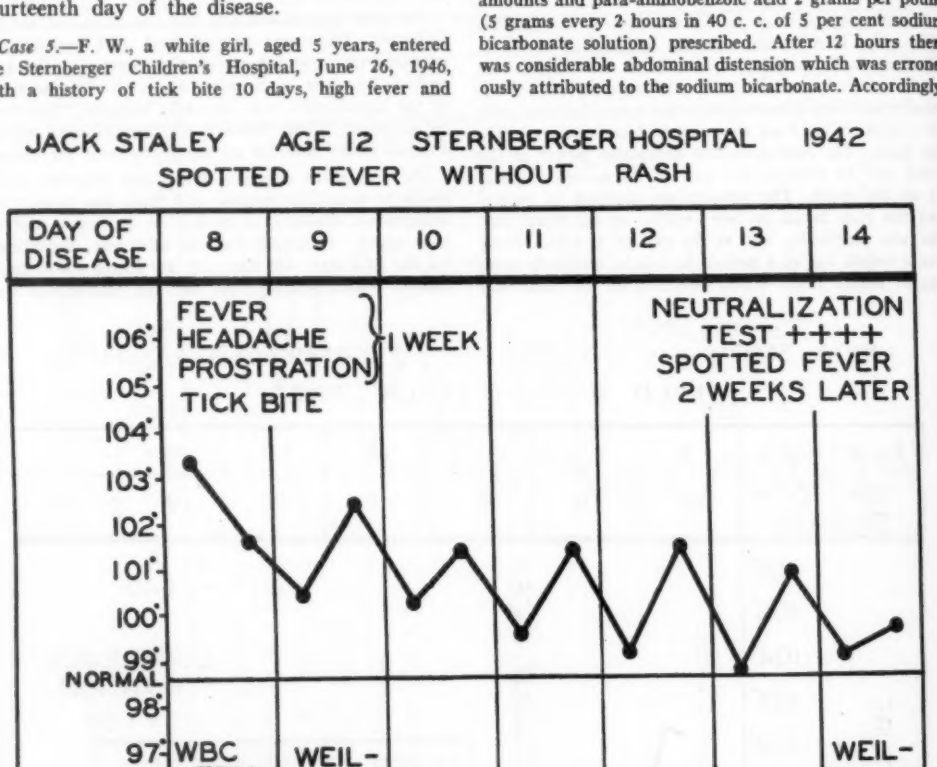

Chart 7
Very mild case without rash before PABA era.

for the next 12 hours this was reduced to 40 c. c. of 2.5 per cent solution to each 5 grams of para-aminobenzoic acid. The next morning the clinical impression of acidosis was proved correct by a blood carbon dioxide combining power of 31 volumes per cent. The para-aminobenzoic acid blood level was 65 milligrams per 100 c. c. Acidosis was corrected with sodium lactate solution and the para-aminobenzoic acid reduced to 2 grams every two hours. The next morning the blood level was 120 mg. per cent and administration of the drug was stopped. That evening the child went into a virtual collapse. The serum protein level which had been 6.4 grams on admission was found to be only 3 grams per 100 c. c. She was given 25 grams of serum albumin (obtained by courtesy of Dr. George Harrell) intravenously and later was given plasma in large amounts. On the fifth day the para-aminobenzoic acid blood level was 80, serum protein 5.38 grams and the temperature normal, but the child looked sick and was delirious. That evening fever and signs of heart failure developed, and by the next morning lobar solidification was present in the right lung. The para-aminobenzoic acid blood level was found to be 0. Para-aminobenzoic acid ¾ gram per pound, digitalis and penicillin were given. After four days of high fever the para-aminobenzoic acid level was 30 mg. per cent and the dose was increased to 1 gram per pound. The temperature dropped to normal in three days and the child made an uneventful recovery from then on. Blood obtained July 10 agglutinated B. Proteus OX19 1:320 and showed complement fixation positive 1:4 for Rocky Mountain spotted fever.

This patient was improperly handled in several respects: (1) too much para-aminobenzoic acid was given and intoxication resulted; (2) too little sodium bicarbonate was used to buffer the para-aminobenzoic acid with the result that acidosis was produced; (3) para-aminobenzoic acid was stopped too soon, the blood level fell to 0 overnight and a relapse with heart failure and pneumonia developed. When proper amounts of the drug were then given, rapid recovery ensued.

Case 6.—L. H., a white girl aged 5, was admitted to the Sternberger Children's Hospital on May 29, 1946, with a history of tick bite, fever, chills and prostration 8 days, a rash 6 days, delirium 3 days.

Examination revealed a critically sick, dehydrated child with a hemorrhagic rash all over the body and face with maximum intensity on the extremities, moderate edema of the face and feet, conjunctivitis, palatal enanthema, a few rales at the right lung base, a pulse rate of 150, an enlarged spleen and the liver palpable just below the costal margin. The white blood cell count was 7,000, hemoglobin level 11 grams, urinalysis positive for albumin and a few granular casts. The Kahn test was negative as was agglutination against Proteus OX19. The serum protein was 4.4 grams per 100 c. c.

Dehydration was overcome with glucose in lactate-ringer's solution intravenously, and the serum protein was restored to normal and maintained there by injections of plasma at appropriate intervals. The signs of heart failure, suggestive on admission, became obvious after 24 hours, and digitalis and oxygen were employed. Para-aminobenzoic acid was given during the first week in doses which varied from 1 to 2 grams but at 4 hour intervals (1/5 to 1/3 gram per pound of weight per 24 hours). The para-aminobenzoic acid blood level during this time varied from 6 to 11 mg. per cent. Signs of lobar consolidation developed, the fever continued, and the child remained critically ill. On the eleventh day para-aminobenzoic acid was increased to ¾ gram per pound and the blood level fluctuated from 14 to 39 mg. per cent until it was discontinued on the seventeenth day. The temperature receded by gradual lysis, and the child recovered slowly. The rash remained deeply hemorrhagic and on the extremities became confluent in patches, some of which sloughed. Blood collected on the fifteenth day agglutinated B. Proteus OX19 in a dilution of 1:640 and yielded a complement fixation test positive 1:32 for Rocky Mountain spotted fever.

The poor result in this patient (the first to be treated with para-aminobenzoic acid) was obviously due to the very small dose administered (1/5 to 1/4 gram per pound) and to the 4-hour interval between doses. The drug is excreted with such rapidity that a two-hour interval is essential in order to maintain an adequate concentration in the blood and tissues.

In none of these six patients was any difficulty encountered in administering the para-aminobenzoic acid, but gavage may be necessary in unconscious patients. The drug was given in cold 5 per cent sodium bicarbonate solution. Acidosis developed in a patient whose dose of para-aminobenzoic acid was too great (3 grams per pound) and was not adequately buffered with sodium bicarbonate solution. White blood cell counts were made at frequent intervals on every patient, but in no instance did leukopenia develop. The impression was obtained that abdominal distension and some degree of delirium were possibly due to para-aminobenzoic acid. Several patients continued to be irrational after becoming afebrile and in each instance the sensorium cleared as soon as administration of para-aminobenzoic acid was stopped.

Edema is a feature of severe spotted fever, and recovery is regularly accompanied by considerable weight loss. Three factors probably account for this edema as Harrell, Venning and Wolff[3]

point out: an inflammatory extravasation of fluid into the tissues due to widespread vascular damage, hypoproteinemia, and heart failure.

The striking thing about these patients was the amazing speed with which fever dropped, rash faded, and recovery ensued in five of the six cases as soon as adequate blood concentrations of para-aminobenzoic acid were achieved. The sixth patient received far too little of the drug materially to affect the course of her disease.

TREATMENT PLAN

The following comprehensive plan is proposed for the treatment of Rocky Mountain spotted fever:

(1) The fluid and electrolyte balance should be restored to normal by means of intravenous injections of glucose in saline or lactate-ringer's solution. It should then be maintained at the normal level by oral intake of fluids and added sodium chloride. It has been pointed out by Harrell, Venning and Wolff[3] that intravenous injections of electrolytes in solution in a patient whose serum protein is too low will serve only to produce more edema and possibly circulatory failure with pulmonary edema.

(2) Acidosis should be corrected by intravenous and subcutaneous injections of sixth molar sodium lactate solution in appropriate dosage.

(3) The serum protein level of the blood depleted in this disease by starvation, vascular damage and liver failure should be restored to normal by intravenous injections of plasma (and, in emergencies, of serum albumin). This level should be maintained by further injections of plasma at appropriate intervals and by a high protein diet (fed by gavage if necessary). If anemia develops blood should be given freely. (Transfusion from a donor convalescent from spotted fever is of no particular advantage).

(4) A very high intake of vitamins should be furnished by mouth, by gavage or parenterally if necessary. Thiamin is given to help prevent shock, ascorbic acid to obviate blood vessel endothelial damage, vitamins B complex and K for liver damage and increased prothrombin time.

(5) One-half to 1 gram of para-aminobenzoic acid per pound of weight per day is given, depending upon the size of the patient. Small children get 1 gram per pound; very large ones half this much; the intermediates about 3/4 gram. This is partially buffered with 10 c. c. of a 5 per cent solution of sodium bicarbonate per gram in order to prevent acidosis and nausea and is given at two-hour intervals. The blood level should be estimated[14] each day at approximately the same time with reference to a dose of the drug. Thirty to 60 mg. per 100 c. c. is desirable; 60 to 80 may be necessary to obtain the best results; above 80 may be hazardous. Administration of the drug is usually continued for four or five days after the temperature has reached normal.

(6) The possible effects of para-aminobenzoic acid should be watched for: acidosis, leukopenia, abdominal distension, delirium. If the white cell count falls below 3,000, para-aminobenzoic acid should be discontinued. Tympanites and delirium occur fairly frequently but are probably of little importance.

(7) The complications of spotted fever should be carefully looked for: congestive heart failure (for which oxygen and digitalis in full doses are helpful); pneumonia (usually lobar, probably rickettsial, ordinarily not helped by penicillin which is always given); encephalitis; thrombophlebitis. The heart failure is usually reversible and when recovery occurs it is complete.

(8) It is possible but extremely difficult to treat these patients without adequate laboratory control. Frequent determinations of the carbon dioxide combining power, serum protein and para-aminobenzoic acid levels of the blood are virtually a necessity, while non-protein nitrogen and chloride blood levels and prothrombin time determinations may be valuable aids.

(9) It would be extremely helpful if a soluble preparation of para-aminobenzoic acid were available for parenteral injection in order rapidly to initiate treatment in the unconscious or vomiting patient. So far such a preparation is not available.

SUMMARY

The morbidity and mortality of Rocky Mountain spotted fever in this section is discussed.

The development of rational and properly controlled supportive therapy in this disease is related.

The experimental and clinical background for the use of para-aminobenzoic acid in spotted fever is described.

The histories of six consecutive cases of spotted fever treated with para-aminobenzoic acid are reported.

A comprehensive plan for the treatment of Rocky Mountain spotted fever is outlined which combines properly chosen and adequately controlled supportive therapy with the administration of para-aminobenzoic acid.

CONCLUSIONS

(1) Rocky Mountain spotted fever is a common, serious and often fatal disease in this section of the country.

(2) Intelligently chosen and properly controlled supportive therapy is extremely helpful.

(3) When para-aminobenzoic acid in adequate dosage is combined with proper supportive therapy a rapid and brilliant therapeutic triumph is usually achieved.

(4) The results obtained in these six patients suggest that deaths from this fearful disease may be practically eliminated by such combined therapy.

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DISCUSSION (*Abstract*)

Dr. Warren W. Quillian, Miami, Fla.—Many of us are prone to think of the rickettsial diseases as a vague group of clinical conditions, not very well classified, and transmitted to man by a louse, a tick, or a flea. Epidemic typhus, Rocky Mountain spotted fever, and "Q" fever are good examples of the rickettsial diseases observed in this country. Yet, until comparatively recent times, there has been the feeling that such conditions are geographically isolated; occurring only in Montana, the Rocky Mountain area, or some other distant region. We are grateful to the essayist, who has emphasized the increasing incidence of these diseases in the South and Central Atlantic states.

The public health significance of Rocky Mountain spotted fever should be stressed. Until the advent of para-aminobenzoic acid therapy, case fatality rates were high. But the drug can be abused. Adequate blood concentrations are essential for optimal results. Rapid excretion can be overcome by frequent administration. Proper buffering with sodium bicarbonate is necessary in order to avoid acidosis. And laboratory controls are as important as sufficient dosage for intelligent supervision and maximum benefits. The sulfonamides are not only useless, but probably harmful if used concurrently with para-aminobenzoic acid. Strict supervision of the relationship between fluid intake and output is very important in the management of these cases.

In areas where the incidence of Rocky Mountain spotted fever is high it has been found practicable to immunize large groups of the population by the inoculation of a killed suspension of the specific rickettsia. This vaccination appears to reduce the incidence and severity of the disease, when repeated annually among those likely to be exposed. Ticks should be removed from dogs with forceps or a piece of paper rather than with the unprotected fingers. The hands should also be carefully washed with soap and water after contact with them.

Interest was stimulated during the recent war in tsutsugamushi disease, a form of scrub typhus transmitted to man by a trombiculid larval mite. The malady is endemic in large areas of the Southwest Pacific. When our troops became infected, early diagnosis was vital, because our medical officers were forced to rely upon rest and general supportive measures alone, in the absence of any specific or chemotherapy. Following the experimental and research efforts of Snyder, Anderson,

Grieff, Hamilton, Yeomans and others, from 1942 to 1945, clinical application of their results was undertaken. Tierney, in May 1946, summarized his experiences with para-aminobenzoic acid in tsutsugamushi disease studied at the 20th General Hospital and the 94th Indian General Hospital in northern India and Burma. In a series of 34 cases, to which reference was made by Dr. Ravenel, 18 were treated with large doses of para-aminobenzoic acid; and their clinical course was compared with 16 alternate controls who received only general supportive treatment. Those who were given para-aminobenzoic acid had few complications, less severe course, shorter convalescence and a lower case fatality rate.

Since most of the rickettsial diseases have a general basic pattern, the effect of para-aminobenzoic acid in Rocky Mountain spotted fever and in tsutsugamushi disease may open a new line of therapeutic attack upon others of the group of rickettsial diseases for which there has been no cure.

Dr. Arthur H. London, Jr., Durham, N. C.—The discussion of the eastern variety of Rocky Mountain spotted fever has now lent itself to a division into approximately four phases. First, the revolutionary work of Dyer and Rumreich in calling our attention to the fact that many of the cases that we were prone to call typhus fever occurring on the Atlantic Coast were actually cases of Rocky Mountain spotted fever. The next phase was the work of Harrell and his associates in pointing out the importance of fluid balance, the use of plasma, and in stressing the damage that is done to the capillaries by this disease.

The third phase was the work of Schneider and his associates in pointing out the use of para-aminobenzoic acid in the treatment of the rickettsial diseases, and finally, the fourth stage, this very delightful work of Dr. Ravenel in giving us a comprehensive summary of the treatment of Rocky Mountain spotted fever. The comprehensive plan of Dr. Ravenel should become a routine in the treatment of Rocky Mountain spotted fever.

The early diagnosis of spotted fever is extremely important. Sometimes we get children in the hospital without a history of tick bite who are extremely ill, prior to the onset of a characteristic rash. It is important to search diligently all children who may have been exposed to the disease. Sometimes a tick is found in unusual cases. In one of my patients we found the tick down in the ear canal holding on very tightly to the ear drum. A day or two later he developed the characteristic rash.

I wonder if in Dr. Ravenel's plan it would not be a good idea to add rutin along with the vitamins, with the idea that in cases which do not recover so rapidly as his seem to have, it will have some effect on the capillary permeability. It certainly seems that a fifth phase of this disease is most important, mentioned by Dr. Quillian, and that is its prevention. In certain areas in the country, this disease appears endemic. We say it is endemic to a state. However, in certain sections there are many more cases. In the section from which Dr. Ravenel comes the majority of cases for North Carolina were reported. It would seem that extensive immunization in these areas would be the ideal plan.

Dr. George T. Harrell, Winston-Salem, N. C.—Dr. Ravenel allowed us to study some of the cases he saw this year and to observe the excellent results which can be obtained by a clinician experienced with the disease. He gave us permission to determine the blood volume and extravascular thiocyanate space to parallel work under way in our own clinic. The comment has been made that the cases in North Carolina are not severe; Dr. Ravenel's statistics and the appearance of the patients as shown by the lantern slides would seem adequately to refute this statement. The North Carolina strain of Rocky Mountain spotted fever is highly virulent.

With the introduction of para-aminobenzoic acid it becomes more than ever important to differentiate specific therapy, including antiserum, from supportive therapy. Since theoretically PABA acts by increasing the metabolism of cells, thus creating a competition between the rickettsia and host cells, even more attention must be paid to supportive therapy than has been accorded it in the past. PABA is one of the B vitamins and large doses of it may depress the activity of other members of the B complex, unless all are given in large amounts. Since protein has also been shown to be an important part of supportive therapy, the intake of both proteins and vitamins should be greatly increased. It should be stressed that PABA, as well as antiserum, is only an adjunct to supportive therapy.

We believe that penicillin should be given at the earliest detection of signs of pulmonary involvement, since the majority of the patients who die have some evidence of pneumonia. Penicillin is a relatively non-toxic drug and will help to control infection due to the ordinary respiratory tract-born organisms which can be recovered from the lungs of patients with Rocky Mountain spotted fever.

Even when vitamin K was given orally, we have noted instances of deficient prothrombin formation, detected by the presence of petechiae when a tourniquet was applied. In most cases parenteral administration of menadione resulted in prompt return of the prothrombin time to normal; in one instance, however, it was necessary to add methionine to the oral therapy before a response occurred.

As Dr. Ravenel has indicated, peripheral circulatory collapse and central myocardial failure must be carefully differentiated, since the treatment of the two conditions is radically different. One can frequently anticipate by laboratory studies the full development of complications in the circulation and initiate therapy before they are far advanced.

We believe that the chick-egg vaccine should be administered routinely in heavily endemic areas and in areas where the strain of rickettsia is especially virulent

and cases are severe. As Dr. Ravenel has pointed out, the disease is spotty in distribution, so that recommendation for routine vaccination should be made on the basis of the local situation.

Dr. Ravenel (closing).—Dr. London reported the first case of Rocky Mountain spotted fever in North Carolina, and Dr. Harrell and his associates were responsible for the brilliant pioneer studies in the pathologic physiology of this disease.

Both Dr. Quillian and Dr. Harrell mentioned the prophylaxis of spotted fever with vaccine. It seems that PABA now offers an additional hope of prophylaxis in that in experimental animals those given PABA and then infected with spotted fever do not contract the disease. I think it is perfectly rational in case an unvaccinated patient has been bitten by a tick in a heavily endemic area, to administer PABA prophylactically. Those of us in this part of the country will probably do that regularly from now on.

A DISCUSSION OF THE COMMON MENINGITIDES AND THEIR TREATMENT*

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In the past few years with the advent of the sulfonamides and, more recently, penicillin and now streptomycin, rapid strides have been made in the treatment of the pyogenic meningitides. We thought that it would be interesting to review briefly the different types and treatments of pyogenic meningitis seen in children. Since the various organisms causing meningitis, and since the history, physical findings and therapy of these patients differ, it will be necessary to describe the treatment of each separately. In order to present this paper in the time allotted, we thought that the more common types of meningitis, namely: tuberculous meningitis, meningococcic meningitis, pneumococcic meningitis and influenzal meningitis, should be considered.

In tuberculous meningitis the onset is usually slow, varying from 5-6 days to as long as 2-3 weeks. During this time, the child develops anorexia, becomes irritable and may be constipated. He does not play as usual and there are periods of drowsiness. Also, there may be frequent vomiting, which is apparently without cause. Fever, if present, is usually low-grade in character. As the disease progresses the drowsiness becomes more marked. Convulsions occur, but only rarely. Evidence of meningeal irritation, such as stiffness of the neck and back, increased reflexes and positive Kernig and Brudzinsky signs are usually present. As time goes on, the patient develops athetoid movements and spasticity develops in the extremities, which frequently changes from one to the other. The pupils may be dilated, contracted or unequal. The drowsiness passes into a stuporous state, and, finally, into coma, from which the patient cannot be aroused. There may be a terminal rise of temperature to 106-107° F. Lumbar puncture reveals from 50-100 cells per cubic mm. with a predominance of lymphocytes. The total protein content is high and the quantitative sugar and chlorides are decreased. Careful examination may reveal acid-fast bacilli. Culture or guinea pig inoculation will be positive.

In meningococcic infections there are two types which are seen frequently. Probably the most common form is the meningeal type, which usually has an abrupt onset with general malaise, fever, headache, vomiting and, in younger children, convulsions. In many of these cases, there are petechial lesions scattered over the body and extremities. There are a high temperature and a rapid pulse. The usual signs of meningeal irritation are present. Also, there may be delirium, stupor or even coma. The fontanelle, if open, is full or bulging. Lumbar puncture reveals cloudy spinal fluid, which escapes under increased pressure. The cell count may vary from a few cells to several thousand per cubic mm. The sugar and chlorides are reduced and the proteins increased. Smear of the spinal fluid will usually show gram-negative intra- and extracellular diplococci which are confirmed as meningococci when the spinal fluid is cultured. Early blood culture is frequently positive, especially if petechiae are present.

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The septicemic type is the other form frequently seen. Here we have an acute onset with fever, vomiting, chills or convulsions and an early appearance of petechial or purpuric lesions of the skin and mucous membranes. Examination does not reveal any meningeal signs and lumbar puncture done at this stage is usually negative. If treatment is not instituted the meninges become involved within 24-48 hours. The more severe form of this type is called fulminating meningococcemia. Here the onset is similar to the former, but more severe, and the patient quickly lapses into a state of delirium or coma. The skin lesions are marked and death ensues within 4-48 hours. Frequently, there is no evidence of meningeal involvement. In many of these cases, there is profound shock caused by massive hemorrhage into the adrenal glands which produces a state known as the Waterhouse-Friderichsen syndrome.

Pneumococcal meningitis occurs in infants more frequently than in older children and in a large majority of the cases is secondary to a pneumococcal infection, especially in the middle ear. There is usually a history of an upper respiratory infection for 3-4 days to a week, then sudden increase in fever. Not infrequently, convulsions occur and the child becomes very restless and irritable and, later, drowsy. Examination reveals a bulging fontanelle, frequently otitis media, and stiff neck with positive Kernig and Brudzinsky. The fluid obtained by lumbar puncture is grossly purulent with 90-99 per cent polymorphonuclear leukocytes, the sugar and chlorides are reduced, and the total proteins are elevated. Gram-positive diplococci, which can be typed, are usually easily seen on smear and can be cultured without difficulty.

Influenzal meningitis is also a disease which is seen more frequently in infants. It is, also, in most cases, a secondary type of infection, the primary focus being usually the middle ear. Here we have a history of an upper respiratory infection, in most cases of a week's duration or longer, and a more insidious onset than is present in the pneumococcal type. Frequently, the patient is seen once or twice with a temperature of 102-104° F. and examination reveals nothing more than a severe respiratory infection, with otitis media; and later he is brought to the emergency room because of convulsions. At this time, there may be only minimal signs of meningeal irritation, that is, only questionable stiff neck, or there may be the full-blown meningeal signs. The anterior fontanelle most of the time is full, but in several of our cases has been sunken, apparently due to dehydration secondary to vomiting and inadequate fluid intake. Lumbar puncture reveals purulent fluid with 90-95 per cent polys. The chemical findings are like those found in other types of purulent meningitis. Smear may show many pleomorphic, coccobaccillary gram-negative organisms, or, unfortunately, as is the case at times, diligent search does not reveal organisms present and it is only when the culture is reported that we know the causative organism. Typing of the organism can be done with specific serum in the same manner that the pneumococcus is typed.

It is necessary before we can treat intelligently and scientifically, that we find out definitely the causative organism. This can be done only by performing a lumbar puncture on the patient, and having a complete examination of the cerebrospinal fluid. This examination should include a total and differential cell count, total proteins, chlorides, quantitative sugar, smear for organisms, colloidal gold, Wassermann and a culture.

We have made it a practice in the Pediatric Department, whenever there is a suspicion of meningitis in a patient to perform a lumbar puncture. If the cerebrospinal fluid obtained appears hazy or cloudy, 20-25,000 units of penicillin are injected into the subdural space before the needle is withdrawn, diluting the drug with the cerebrospinal fluid. While this procedure at times is futile, because the organism isolated from the fluid is not affected by the penicillin, we believe that we are ahead of the game, for if a susceptible organism is later identified, we do not have to subject the patient to another puncture so quickly. In addition to this, we immediately start intensive sulfadiazine therapy. The dosage here is rather high, but apparently this is necessary for best results. An initial dose of 2 grains per pound body weight of the sodium salt is given intravenously. We

then place the patient on a maintenance dosage of 3 grains per pound body weight per day, dividing it into six doses daily. This is administered by mouth with equal doses of sodium bicarbonate if the patient is able to retain the drug. If the patient is vomiting, the same dosage is given intravenously using the sodium salt until he can retain it by mouth.

In addition to the above, we have found that practically all of these patients fare better if they are given fluids intravenously and subcutaneously in order to hydrate them and restore their mineral balance. For intravenous use we have been using a solution of 2.5 per cent glucose and one-half normal sodium chloride, while subcutaneously we administer Hartmann's lactate-Ringer solution. If the patient is in a state of shock, frequently it is necessary to give a continuous drip intravenously, adding blood plasma in an attempt to restore the blood volume. If the patient is anemic, whole blood transfusions (10 c. c./lb. body weight) should be given when hydration is adequate. If blood is given before a state of hydration is reached hemoconcentration may result, which would harm, rather than help, the case.

When a diagnosis of tuberculous meningitis is made, there is, at the present time, nothing other than symptomatic treatment that we have to offer the patient. Recently, there have been reports that streptomycin is effective, to some extent, on the tubercle bacillus *in vitro* and in mice and when this drug becomes more available adequate clinical trial in the treatment of this type of meningitis should be carried out.

In meningococcic meningitis and meningococcemia we have used the sulfonamides, including sulfanilamide, sulfapyridine, sulfathiazole and sulfadiazine, with very satisfactory results. The drug of choice is probably sulfadiazine because of its low toxicity. The dosage here is the same as noted above. The question of the use of penicillin comes up at this time, and, although we found it effective against this organism, we believe that the sulfonamides are more effective and that penicillin should not be used alone, but in conjunction with the sulfonamides. The dosage we use in children is 20-30,000 units intramuscularly every 3 hours and 20-25,000 units intrathecally daily until the infection apparently is under control. In cases of meningococcemia the combined sulfonamide-penicillin therapy has been very successful, and, if these cases are treated adequately, the likelihood of spreading to the meninges is minimal. In the cases of fulminating meningococcemia, however, even more vigorous therapy is indicated, combining with the above, adrenal cortical extract, continuous intravenous fluids, blood plasma, and whole blood transfusions.

In pneumococcal meningitis the combination of sulfadiazine with penicillin appears to be the treatment of choice. Here it is necessary that the penicillin be given intrathecally as well as intramuscularly. In several cases a block has developed at the base of the brain, and it has been necessary to inject the penicillin intracisternally. In smaller children, in whom the anterior fontanelle is open, if improvement does not appear to be progressing, we have had very satisfactory results injecting the penicillin into the right and left subdural spaces through the fontanelle. On these occasions we have placed 20,000 units in each subdural space. While we have never tried penicillin alone in these cases, other authors who have, have reported much better results with the combined therapy, and our cases which received the sulfonamides alone or with type specific serum have certainly not shown nearly so satisfactory results. In some cases which do not seem to be responding as desired to the combined therapy, serum should be given.

Probably the greatest advance in the treatment of meningitis has come about since 1939, when Hattie Alexander reported the use of type B anti-H. influenzae serum in conjunction with sulfanilamide in the treatment of influenzal meningitis. At this point, it might be well to remember that this type of meningitis is due to a gram-negative Coccobacillus, H. influenzae, rather than the virus which causes the better known influenza or "flu." Before the development of this serum and the sulfonamides the mortality rate was about 99 per cent. When the sulfonamides are used alone the mortality rate drops to about 90 per cent, but with the use of the rabbit antibody plus the sulfonamides,

Alexander reported a large series of cases in which 75 per cent recovered. The routine we have been using, with what we think are exceptional results, is patterned after that advised by Dr. Alexander. Sulfadiazine is begun as stated before with an initial dose of 2 grains per pound body weight intravenously, followed by a maintenance dose of 3 grains per pound per day divided into 6 doses in 24 hours. As soon as the laboratory identifies the causative organism of the meningitis as type B H. influenza, a continuous intravenous drip of 2.5 per cent glucose and one-half normal sodium chloride solution is started. The serum, which is concentrated rabbit antibody, and is put up in vials containing 25 mg. of precipitable antibody nitrogen, is then administered to the patient, following a skin sensitivity test. The amount used depends upon the sugar content of the cerebrospinal fluid. If 15 mg. per cent, or less, 100 mg. antibody nitrogen is given; if from 15-25 mg. per cent or less, 75 mg. is used; if from 25-40 mg. per cent, 50 mg. is administered and if the spinal fluid sugar is over 40 mg. per cent, 25 mg. of the antibody nitrogen is given. The serum is given intravenously, diluted in normal salt solution over a two-hour period. After 12 hours a sample of the patient's serum is tested in a 1-10 dilution against a suspension of H. influenzae. If capsular swelling occurs, an adequate amount of serum is thought to be present; if no swelling occurs, another 25 mg. of antibody nitrogen is administered. In addition to testing the blood serum for antibody potency, we have also been testing the undiluted spinal fluid for antibodies in the same manner. When the spinal fluid will swell the capsule of the organism we believe a sufficient amount of serum has been administered. From then on, the patient's general response, together with daily spinal fluid examinations, determines whether or not more serum is given. In several cases, which did not seem to be responding satisfactorily, we have given the antibody nitrogen intrathecally, following which, improvement was noted quite rapidly. The intravenous drip has been continued for 48 hours in most of our patients, and usually when the drip is discontinued, the patient is able to take and retain fluids by mouth, although at times we have found it necessary to tube feed the patient for several days. The sulfadiazine is continued until the temperature has been normal for a week and the spinal fluid findings have reverted to normal limits.

It is now possible to obtain streptomycin, and, according to reports, this drug is definitely beneficial in the treatment of influenzal meningitis. We have had a patient with influenzal meningitis who did not respond completely to the serum-sulfadiazine therapy, and following a week's streptomycin therapy she was completely cured. It is difficult to say whether the streptomycin was beneficial here because the patient apparently was beginning to recover at the time the streptomycin was started.

We have reviewed the charts of all patients with pneumococcic, meningococcic and influenzal meningitis admitted to the Pediatric Service of Roper Hospital from 1935 through August, 1946. A total of 201 patients with these diagnoses were admitted during this period. Of these, 145 were colored and 56 white. There were 83 colored males and 62 colored females; 32 white males and 24 white females, making a total of 115 males and 86 females.

In the meningococcic series 55 patients were colored and 38 white. There were 33 colored males and 22 colored females; 20 white males and 18 white females. In the pneumococcic group there were 34 colored and 10 white. There were 21 colored males and 13 colored females; 7 white males and 3 white females. In the influenzal group there were 56 colored patients and 8 white. Twenty-nine were colored males and 27 colored females; while there were 5 white males and 3 white females.

MENINGOCOCCIC, PNEUMOCOCCIC, INFLUENZAL MENINGITIS PATIENTS ADMITTED TO PEDIATRIC SERVICE, ROPER HOSPITAL, 1935—AUGUST, 1946

	All Types		Total	Meningococcic		Pneumococcic		Influenzal	
	Male	Female		Male	Female	Male	Female	Male	Female
White	32	24	56	20	18	7	3	5	3
Colored	83	62	145	33	22	21	13	29	27
Total	115	86	201						

Table 1

In studying the age incidence of these types of meningitis, it is interesting to note that in the meningococcic group of 93 cases only 17 were under 2 years of age, while the remaining 76 were over 2 years old.

In the pneumococcic group 39 cases were under 2 years of age, while only 5 cases were 2 years old or over.

In the influenzal group we find 52 cases under 2 years of age, whereas 12 cases were 2 years old or over.

Studying the diseases according to the month of admission we find that in the meningococcic group the majority of patients are admitted during the late fall, winter and early spring months. In the pneumococcic group this is also true. In the influenzal series, while January produced the greatest number of cases, we find that cases of this type are admitted throughout the year, there being no definite seasonal incidence.

From a year to year standpoint, we find 28

MENINGOCOCCIC MENINGITIS

Ages	Cases	Recovered	Died	Died 48 hours or less
1 month	1	1		
2 months	1		1	
5 months	2	2		
7 months	1	1		
8 months	1	1		
9 months	1	1		
11 months	1		1	1
12 months	3	3		
13 months	1	1		
14 months	2	2		
18 months	2	2		
22 months	1	1		
2 years	10	9	1	1
3 years	10	9	1	1
4 years	12	11	1	
5 years	6	5	1	
6 years	8	7	1	
7 years	9	8	1	1
8 years	5	4	1	1
9 years	7	6	1	1
10 years	4	4		
11 years	5	4	1	1
Total	93	82	11	7

Table 2

PNEUMOCOCCIC MENINGITIS

Ages	Cases	Recovered	Died	Died 48 hours or less
1 day	1		1	
1 month	3		3	2
2 months	4		4	2
3 months	5	1	4	3
4 months	3		3	3
5 months	3		3	2
6 months	3	1	2	1
7 months	3		3	3
8 months	1		1	
9 months	1		1	
11 months	1		1	1
12 months	3		3	2
13 months	1		1	
14 months	2		2	2
15 months	2		2	1
20 months	2	1	1	1
21 months	1		1	1
2 years	3	2	1	1
3 years	1	1		
6 years	1	1		
Total	44	7	37	25

Table 3

INFLUENZA MENINGITIS

Ages	Cases	Recovered	Died	Died 48 hours or less
2 weeks	1		1	
1 month	2		2	
2 months	2		2	
3 months	1		1	1
4 months	2	1	1	
5 months	7	1	6	
6 months	7	1	6	
7 months	9	4	5	1
8 months	6	1	5	
9 months	1		1	
11 months	2	1	1	
12 months	3	1	2	
13 months	1		1	
16 months	1		1	1
17 months	1	1		
18 months	4		4	1
19 months	1		1	1
22 months	1	1		
2 years	5	5		
3 years	4		4	
4 years	1		1	1
6 years	1	1		
7 years	1	1		
Total	64	19	45	6

Table 4

cases of meningococcic meningitis in 1936. During this year, there was an epidemic of this disease in Charleston, and over 200 cases were admitted to Roper Hospital during the months of January, February, March and April. Following this is a relatively quiescent period. Then a period where the disease reaches its peak again, 8 years later. During 1946 we have had no cases of meningococcic meningitis in children. In the pneumococcic group the incidence according to years does not vary much, although in 1943 a high total of 13 patients were admitted. In the influenzal group, there is not much variation from year to year, although the peak of incidence was in 1939.

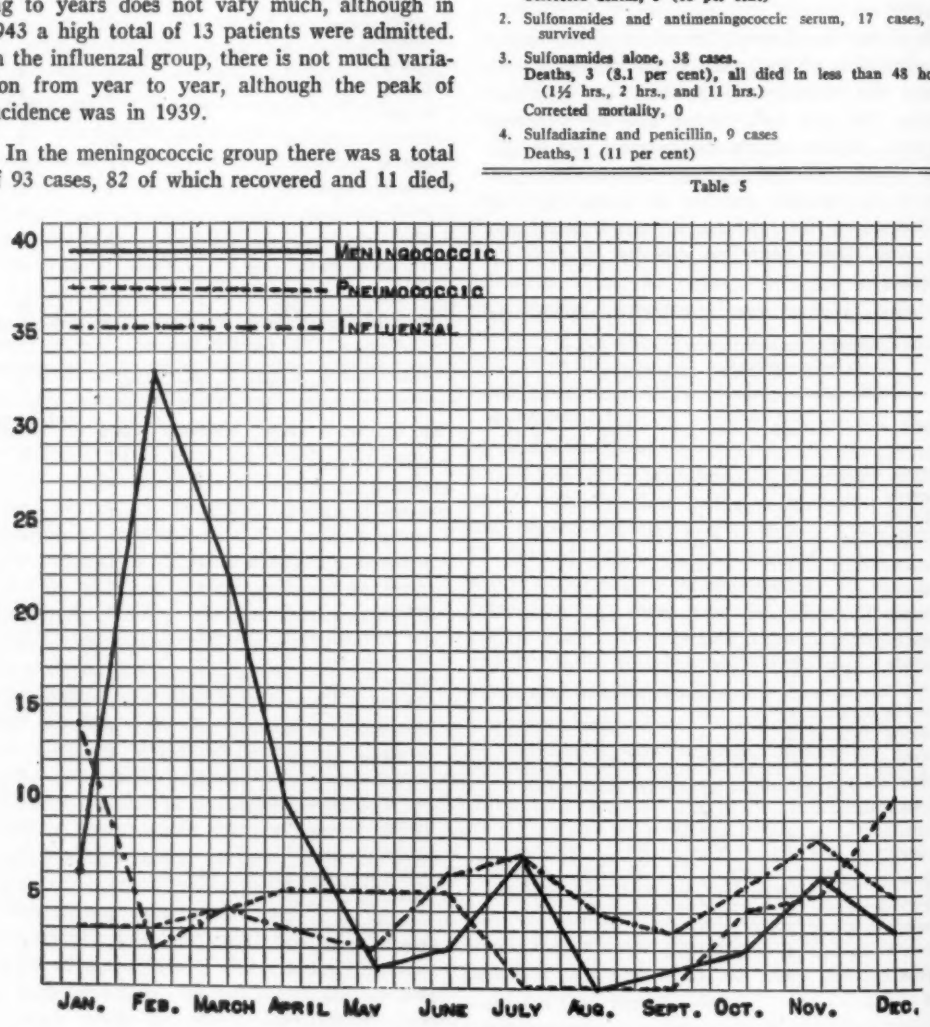
In the meningococcic group there was a total of 93 cases, 82 of which recovered and 11 died,

MENINGOCOCCIC MENINGITIS	
Total	93
Recovered	82 (88.1 per cent)
Died	11 (11.9 per cent)
Deaths 48 hours or less	7
Corrected Total	86
Recovered	82 (95.3 per cent)
Died	4 (4.7 per cent)

Type of treatment

1. Antimeningococcic serum, 29 cases
   Deaths, 7 (24.1 per cent), 4 in less than 48 hours (40 min., 2 hrs., 30 hrs. and 38 hrs.)
   Corrected deaths, 3 (12 per cent)
2. Sulfonamides and antimeningococcic serum, 17 cases, all survived
3. Sulfonamides alone, 38 cases.
   Deaths, 3 (8.1 per cent), all died in less than 48 hours (1½ hrs., 2 hrs., and 11 hrs.)
   Corrected mortality, 0
4. Sulfadiazine and penicillin, 9 cases
   Deaths, 1 (11 per cent)

Table 5

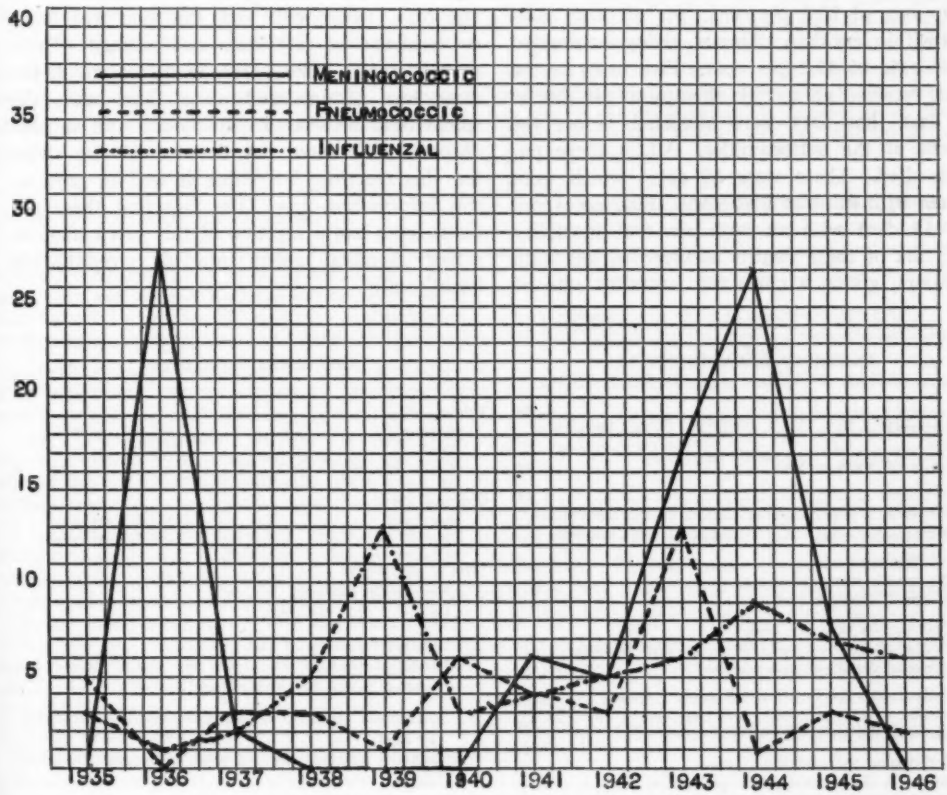


Graph 1

Monthly incidence of meningitis by admission to Pediatric Service, Roper Hospital, 1935-1946.

with a mortality rate of 11.9 per cent. Of these 11 cases which died, 7 died within 48 hours or less. Eliminating these 7 cases, for we do not believe that adequate treatment is possible in such a short period, we have a corrected mortality rate of 4.7 per cent. We have broken down this series according to the type of treatment. In 29 cases antimeningococcic serum alone was used. Seven of these cases died, with a mortality rate of 24.1 per cent. Four of the deaths occurred in less than 48 hours (40 minutes, 2½ hours, 30 hours and 38 hours). Correcting for these cases, we have a corrected death rate of 12 per cent. Seventeen cases were treated with the sulfonamides plus antimeningococcic serum. All of these cases recovered. Where the sulfonamides alone were used and there were 38 cases and 3 deaths with a mortality rate of 8.1 per cent. All of these patients died within less than 48 hours (1½, 2 and 11 hours) respectively, giving a corrected mortality of 0 per cent. Sulfadiazine and penicillin combined were used on 9 cases with one death, resulting in an 11 per cent mortality rate. One of these patients was started on penicillin but showed no response after 48 hours and sulfadiazine was begun. A rapid response to the sulfadiazine therapy occurred and the patient recovered fully.

In the pneumococcic group there was a total of 44 cases. Seven of these recovered and 37 died, with a mortality rate of 84.9 per cent. Twenty-five cases died within less than 48 hours and the corrected mortality rate is 63.1 per cent. Breaking these cases down in regard to treat-



Graph 2
Yearly incidence of meningitis by admission to Pediatric Service, Roper Hospital, 1935-1946.

ment we find that 9 cases had a 100 per cent mortality rate where no specific treatment was used. In 23 cases the sulfonamides alone were used, with 3 recoveries and a mortality rate of 86.9 per cent. In 7 cases the sulfonamides plus type specific anti-serum were used with one recovery and a mortality rate of 85.7 per cent. There were 5 cases on which sulfonamides plus penicillin were used with 3 recoveries resulting in a 40 per cent mortality rate. Correcting these figures for deaths in less than 48 hours, we find a 66.6 per cent mortality on sulfonamides alone. Seventy-five per cent mortality where sulfonamides plus serum were used, and a 25 per cent mortality in the cases where penicillin was used in conjunction with sulfadiazine.

In the influenzal group there were 64 cases, with 19 recoveries and 45 deaths with a mortality rate of 70.3 per cent. Six of these cases died within less than 48 hours, giving a corrected death rate of 67.2 per cent. Five cases in the series received no specific therapy at all, due to the fact that they were admitted before the advent of the sulfonamides. All of these patients died. There were 39 cases which were treated with sulfonamides alone. Four recovered and 35 died with an 89.7 per cent mortality rate. Six of these deaths occurred in less than 48 hours, giving a corrected mortality rate of 87.9 per cent. There were 20 cases treated with the anti-H. influenzae Type B Serum plus sulfonamides. Of these, 15 recovered and 5 died, with a mortality rate of 25 per cent. Two of the cases which died were given an inadequate amount of the serum, and we believe that they should be excluded from the series. This gives a corrected total of 18 cases with 3 deaths and a mortality rate of 16.7 per cent. Of the 15 patients who recovered, 2 received streptomycin, one in the latter stages of the illness, and the efficacy of this drug was doubtful. Another received streptomycin early in the disease with apparently beneficial results. Here it might be of interest to say a few words of our experiences with streptomycin when used intrathecally. To date, we have used it in 4 cases of meningitis, injecting 50,000 micrograms or units daily. In one case, where only one injection was done, no evidence of irritation was noticed. However in the 3 other cases, in all of which the drug was administered more than once, the spinal fluid became grossly bloody and xanthochromic. We have not determined the cause for this reaction, but think it well to pass on this information now. The fact that these patients have had a reaction of this sort makes us rather skeptical about injecting streptomycin intrathecally.

PNEUMOCOCCIC MENINGITIS

Total	44
Recovered	7 (15.1 per cent)
Died	37 (84.9 per cent)
Deaths 48 hours or less	25
Corrected Total	19
Recovered	7 (36.8 per cent)
Died	12 (63.2 per cent)

Type of Treatment

1. No specific treatment, 9 cases
   Deaths 9 (100 per cent)
2. Sulfonamides alone, 23 cases
   Deaths, 20 (86.9 per cent), 14 in less than 48 hours
   Corrected deaths, 6 (66.6 per cent)
3. Sulfonamides and type specific serum, 7 cases
   Deaths, 6 (85.7 per cent), 3 in less than 48 hours
   Corrected deaths, 3 (75 per cent)
4. Sulfadiazine and penicillin, 5 cases
   Deaths, 2 (40 per cent), 1 in less than 48 hours
   Corrected deaths, 1 (25 per cent)

Table 6

INFLUENZA MENINGITIS

Total	64
Recovered	19 (29.7 per cent)
Died	45 (70.3 per cent)
Deaths 48 hours or less	6
Corrected Total	58
Recovered	19 (32.8 per cent)
Died	39 (67.2 per cent)

Type of Treatment

1. No specific treatment, 5 cases
   Deaths, 5 (100 per cent)
2. Sulfonamides alone, 39 cases
   Deaths, 35 (89.7 per cent), 6 in less than 48 hours
   Corrected deaths, 29 (87.9 per cent)
3. Sulfonamides and Type B anti H. Influenza Rabbit Serum, 20 cases
   Deaths, 5 (25 per cent), 2 given inadequate amount of serum
   Corrected deaths, 3 (16.7 per cent)

Table 7

SUMMARY

(1) Establish type of meningitis by identifying causative organism.

(2) In tuberculous meningitis, at the present time, we have no treatment, but there is a possibility that streptomycin may be of value.

(3) In meningococcic meningitis the drug of choice is sulfadiazine, although the other sulfonamides are effective. Penicillin is also a valuable drug in this type of meningitis, but we believe that it is best used in conjunction with the sulfonamides.

(4) In pneumococcic meningitis combined sulfadiazine-penicillin therapy is the treatment of choice. Penicillin should be used intrathecally, as well as intramuscularly or intravenously in this type. In certain resistant cases, type specific rabbit serum may be of value.

(5) In influenzal meningitis the rabbit serum developed by Alexander, together with sulfadiazine, is the treatment of choice. Streptomycin is giving promising results at the present time.

DISCUSSION (*Abstract*)

Dr. Frank B. Schley, Columbus, Ga.—Dr. Beach's beginning treatment for all forms of meningitis is certainly advantageous and desirable but it would be a little difficult to accomplish routinely, except where one practiced only in a department of pediatrics.

In meningococcus meningitis, I feel that sulfadiazine, given intravenously when necessary, is the drug of choice, not only because of its low toxicity, but also because of its superior ability to enter the spinal fluid from the blood in higher concentrations than the other sulfonamides and its greater antibiotic effect upon the meningococcus.

In our experience, we have not found the use of penicillin necessary, but it does give a greater sense of security in the feeling that more than one approach is being made toward the extermination of the infection. In meningococcus meningitis we have also found a daily lumbar puncture unnecessary except to relieve painful intracranial pressure. In fact, a diagnostic and dismissal lumbar puncture have been adequate in several cases since the advent of sulfadiazine, and are much less disturbing to the child.

In our two autopsied cases of Waterhouse-Friderichsen syndrome we had not time to instigate any treatment before death intervened. In one case the blood pressure was so low that a blood count could not be obtained because of lack of bleeding from the needle puncture.

Our only comment on pneumococcus meningitis has to do with a case in which treatment was stopped and the patient sent home without further treatment when the spinal fluid became normal. This same patient returned a week later with the same complaint and died. The patient was obviously dismissed too soon or had a reinfection from the undiscovered original source.

Influenzal meningitis has been a very deadly disease in my limited experience until the sulfonamides, the anti-influenza serum, and streptomycin became available. We had a recovery with sulfathiazole when it was first available, and about nine months ago a case that recovered after one intramuscular injection of 100 mg. of antibody nitrogen, followed thereafter by only supportive and symptomatic treatment.

In July, 1946, a soldier's baby was referred to Fort Benning, Georgia, Hospital, where streptomycin was available, and it recovered after twelve treatment days of streptomycin, 100,000 units intramuscularly every three hours until 9,300,000 units were given. This was combined with supportive and symptomatic treatment.

I believe there will be a great deal of improvement in the mortality of influenzal meningitis when this form of treatment has had more usage.

Dr. Beach's vital statistics are interesting both as to the predominance of meningitis in males, in the colored race, and in the age incidence. It certainly seems that hygienic surroundings have an influence upon the occurrence of the disease.

It may be of interest to report that we successfully treated a three-weeks-old infant with meningococcus meningitis who had never been out of the room he was born in until he was taken to the hospital for treatment.

GEORGIA'S COMMUNITY-WIDE SURVEYS*

CHEST X-RAY; BLOOD TEST AND DENTAL

By LESTER M. PETRIE, M.D., M.P.H.†
Atlanta, Georgia

Within the past year, since October 1945 in community-wide surveys in the Savannah, Columbus, Macon and Augusta areas in Georgia, we have done chest x-ray and blood test examinations of about 215,000 persons out of a total estimated population of 438,000 persons of all ages. The overwhelming majority of those examined were over 12 years of age.

We have probably examined more than 60

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†Director, Division of Industrial Hygiene, Georgia Department of Public Health.

per cent of the entire adult population of these areas. Apparently, we examined more adult Negroes in the Savannah area than there were according to the 1940 census, and over 90 per cent of them based on the 1943 ration coupon records. This was success beyond our fondest expectations, especially when it is remembered that the entire program was voluntary.

We have been doing chest x-ray surveys of individual industries in Georgia since 1942, and even an occasional combined x-ray and blood test survey in industry. Large scale x-ray surveys and also large scale blood test surveys have been done elsewhere. But never before anywhere had a combined chest x-ray and blood test survey on a comparable scale been attempted.

The enthusiasm of survey workers and general public alike is hard to describe. Those who have not experienced it cannot appreciate it.

For many there is no such thing as fixed hours of work. Eight a.m. to midnight is nothing unusual. A missionary zeal pervades. The people believe in the work. Who ever thought he would see Negroes lined up, many hundreds in line at a time, waiting sometimes for hours to have needles pushed into them to draw blood, and all voluntary? I saw them close the doors on a line of over 500 Negroes one night at Yamacraw Village in Savannah, at about 9:00 p.m., because sterile needles had given out for the day. We had 3,000 needles at the time, but had to secure more to take care of the demand. During the third week of the survey in Savannah, about 3,600 people were examined daily and the average for the 45 days of the survey was more than 1,500 per day.

I have seen marvelous cooperation between Negroes and whites. In all these cities in Georgia, I have seen white and colored physicians working side by side; white and colored nurses working side by side; white and colored clerks working side by side; yes, and white and colored employes in industry and white and colored citizens at public stations going through the same lines for blood tests and chest x-rays. All voluntarily working harmoniously together in common effort for the common good.

After seeing it work, I am convinced that the combined survey adds to the effectiveness of both the venereal disease and the tuberculosis case finding. For example, certain well-to-do persons who might not consider or who might even resent the suggestion that they go to a public survey center to have a blood test for syphilis, may appreciate the opportunity of having the chest x-ray, and accept the blood test as a corollary to the survey. Some of them even may be keenly sensitive to this opportunity to settle suppressed fears they may have concerning the status of their own blood, without any probability of embarrassment to themselves, unless the test should be positive.

In each community which we have surveyed to date we have had either five or six examining units located at strategic points to make the examinations readily available to everyone. Each unit consists of a photofluorographic chest x-ray machine and the required number of clerks, technicians and nurses to make out the records, take the x-ray pictures, and draw the blood. For the convenience of industry one complete portable unit of this nature is moved directly into the industrial plant. The employes are examined on a previously worked out schedule with minimum loss of time from work. The examinations are readily performed at a rate of 100 per hour. The usual schedule calls for 25 employes to report for examination every 15 minutes. Pictures are taken through the clothing.

Dental studies have been added to the last three surveys. This is a research project not particularly concerned with control procedures at present but designed to determine dental needs of a cross section of average typical adults. As we have had only one dental chair, this study has been conducted each day at only one of the five or six examining units, 20,599 individuals having had dental examinations in Columbus, Macon and Augusta.

The 70-millimeter chest x-ray pictures also bring to light many cases of previously unrecognized pathology not necessarily of tuberculous origin such as abnormalities of the heart, aneurysm, tumors, non-tuberculous pulmonary disease, and the like.

Every individual examined is given a confidential report of the findings in his case. If nega-

tive, he receives negative reports by mail a few days after the examination. If there is any suspicion of disease or if a test is unsatisfactory he is asked to report to the health department. Here he is given confirmatory tests as indicated, such as repeated blood tests, sputum examinations, large x-ray, tuberculin test. A detailed medical history is taken. He, together with the evidence which has been collected, is examined by a physician, a specialist in chest or venereal disease. He is told confidentially of the findings and is given authoritative advice as to the need for treatment. If treatment is indicated he is asked to name the physician of his choice. All examinations are strictly confidential. Blood specimens and x-ray pictures are identified by number rather than by name. No reports identifying any individual are given by the health department to anyone except the individual concerned and the physician of his choice.

Where cases of non-tuberculous or non-venereal disease are found which tie in with other activities of the health department, use is made of the new knowledge if possible. For example, when cases of silicosis are found, as they have been among foundry workers and granite cutters, this information is used by the Industrial Hygiene Division, and correlated with industrial hygiene survey dust counts and the like. Nevertheless, confidential treatment of the information with regard to the individual is not broken. A statistical summary of survey findings of any particular plant, giving the number of individuals examined and the number whose tests were positive, doubtful, or negative, may be given to plant management, but personal findings of any individual will not be identified to anyone except the individual concerned and the physician of his choice.

Case finding is not enough for a complete program. Unless the infectious cases are rendered non-infectious our objective of breaking the chain of infection among our people is not attained. This makes it necessary that treatment be provided for those infectious individuals not able or willing to secure treatment from their private physician at their own expense.

The two original rapid treatment centers for syphilis operated by the United States Public Health Service in Georgia, one near Savannah and the other at Augusta, were available to us for treatment of cases found in the earlier surveys. Effective August 1 of this year, however, we opened the state-owned and operated rapid treatment center in Alto State Hospital, (which had formerly been our state tuberculosis sanatorium). The other two rapid treatment centers were closed as soon as the case loads could be effectively transferred. With a bed capacity of about 750, there are 588 beds in service. During the first two months of operation 2,000 patients were treated. The venereal disease control budget is roughly $1,000,000 this year in addition to special survey expenses.

For the treatment of tuberculosis, the State Health Department early in 1946 acquired Battey State Hospital at Rome, Georgia. This was formerly Battey General Hospital of the U. S. Army. It has a potential capacity of 3,000 beds, making it one of the largest tuberculosis hospitals in the country. Our state legislature has increased the annual appropriation for maintenance of our tuberculosis sanatorium from $540,000 last year to $1,540,000 of state funds this year. This appears to be sufficient to maintain 1,500 beds for a year, or 3,000 beds for 6 months. The above appropriation does not include the additional appropriation of state funds for general public health which has been increased from $600,000 last year to $2,100,000 in 1946. It is interesting to compare the last appropriation with the $104,000 of state funds which the department received in 1936.

The exodus from Alto State Hospital to Battey was a great event. Additional tuberculosis patients are now being admitted at the rate of about 30 each week and sufficient doctors and nurses have been secured to care for this increasing patient load for the remainder of 1946. On October 3, there were 785 patients being cared for at the institution. By the end of the year more than 1,000 are expected. The facilities of the hospital are still designed for service to curable cases which offers the greatest amount of good to the largest number of people. Still, a minimum number of far advanced cases that are public health problems are accepted.

We do not want to leave the impression that

we have found the final solution to all problems of syphilis and tuberculosis control, nor that our program is easy. Neither objective has been attained but we do believe our program is more effective than anything we have previously been able to devise. Time does not permit me to discuss all the inherent difficulties of administration, which have strained almost to the breaking point the combined resources of the U. S. Public Health Service, the state and local health departments, with the assistance of the tuberculosis associations, medical societies, and local civic groups.

Problems which should be successfully met include securing the approval and cooperation of the medical society and of local government; correlation of the survey with local health department services; housing, transportation, and communication; publicity; community organization, white and colored; industrial organization; supervision, coordination, and supply of all units; operation of blood test laboratory; records; confidential reports to each individual; epidemiological follow-up of case contacts; industrial hygiene follow-up in dusty trades; treatment and rehabilitation of cases, and sometimes of families. When the survey teams leave at the end of the survey, the community problem of correcting defects found has just begun.

The information is not yet available as to many details of costs and findings especially in the later surveys. For the Savannah survey an estimate of $77,000 has been made, which averages about $1.07 per person examined.

In Savannah and Chatham County, 71,149 individuals were blood tested by the Mazzini rapid slide precipitation method. Confirmatory studies, including standard Kahn tests, were made of all cases or suspects. There were 10,549 confirmed cases of syphilis and 226 cases of gonorrhea identified. Of the syphilitics, 6,781 cases were already known to treatment, while 3,768 were previously unknown as syphilitic to themselves or anyone else. In other words, by the survey technic, we discovered or rediscovered more than half again as many cases of syphilis as the combined resources of the local medical and public health professions had uncovered with all their previous efforts.

The 3,768 previously unknown cases of syphilis may be classified by stage of disease as follows:

Primary	20	(0.5 per cent)
Secondary	51	(1.4 per cent)
Early latent	641	(17 per cent)
Other or unknown	3,056	(81 per cent)

Over 100 of these were asymptomatic neurosyphilis.

Within four months time after completion of the survey in November 1945, treatment of 2,370 of the previously unknown cases of syphilis had been completed at the Southeastern Medical Center rapid treatment hospital on Oatland Island. The majority of the remaining previously unknown cases either secured treatment from their personal private physicians or were already permanently non-infectious cases whose treatment is not a public health responsibility.

Also in Savannah and Chatham County 67,961 individuals were examined by chest x-ray. The following diagnoses were arrived at:

66,924	or 985	per 1,000 were considered negative.
438	or 6	per 1,000 were confirmed tuberculosis.
90	or 1	per 1,000 were suspected tuberculosis.
30	or ½	per 1,000 were characteristic or calcification.
343	or 5	per 1,000 were non-tuberculous pathology.
68	or 1	per 1,000 were suspected tuberculosis by small film but no follow-up.
68	or 1	per 1,000 were non-tuberculous pathology by small film but no follow-up.

Most of the 438 cases and 90 suspects of tuberculosis were unknown before the survey. As of February 11, 1946, there were 848 cases and suspects listed on the central case registry in the health department, but 61 per cent of the cases were unknown to themselves or anyone else prior to the survey.

Of the 438 confirmed cases, 125 were diagnosed active, 178 questionable activity, and 135 inactive. By April 1946, less than five months after the survey, 68 cases had been hospitalized out of 73 for whom hospitalization had been requested. Only 2 patients refused (one was a Christian Scientist) and the remaining 3 were not hospitalized for other reasons. At least 9 additional individuals had been hospitalized for treatment of non-tuberculous pathology found by the survey.

The 1940 census gives the population of Georgia as 3,123,723. If the known tuberculosis case load at Savannah at the end of the survey is an index of what a survey of this

entire state population would reveal, we might anticipate the identification of 17,500 cases or suspects in Georgia by this method.*

Before the advent of mass chest x-ray technics we could estimate the number of cases of active tuberculosis in a community from the estimated ratio of 9 cases per annual reported death. On this basis we would estimate 12,447 active cases in Georgia. We knew these cases existed but in many instances did not know who they were.

With mass x-rays we can determine how many and also identify them, who and where they are.

Those of us here who have dedicated our lives to the public health are facing one of the most challenging opportunities ever offered to preventive medicine. Ahead of us in the foreseeable future is the pay-off for which many of our predecessors have labored. Koch discovered the tubercle bacillus in 1882. During his century one-fourth of the population of Europe died of consumption. At the very time he was making his discovery the death rate from tuberculosis in the U. S. registration area was 390 per 100,000 population. But now, today, the picture is different. Tuberculosis is no longer the Captain of the Men of Death in our country but has been reduced to eighth place. The death rate from tuberculosis in Georgia last year was 35.5 per 100,000 population. And now medical science has placed these new and potent weapons in our hands, weapons with which we can wipe out tuberculosis in our time, reduce the erstwhile captain to a minor rank similar to that of smallpox, yellow fever, or diphtheria. If we do this, we will have justified all expenditures ever made for public health work.

We in Georgia have found the combined mass survey technic more effective than any previous case finding method. The surveys are probably only a transition to even better methods, but for the moment we believe they should be extensively used wherever there are facilities for follow-up of cases and contacts, for care of cases found to need treatment, and for rehabilitation of not only the case but his broken family as well. Let us of the medical and public health professions unite with workers in related agencies, and finish this job in our time, that our children may have health.

*Many variables must be considered which make this estimate not too reliable, such as: the proportion existing between previously known and unknown cases; the discovery rates; population distribution as to color, sex, and age; efficiency of the survey; geographical variations; etc.

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SODIUM CHLORIDE AND FLUID REPLACEMENT IN TREATMENT OF MALARIA*

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Sodium chloride depletion and dehydration are factors which should be considered in the treatment of malaria. Much has appeared in the literature during the last few years concerning specific therapy of malaria but non-specific or supportive measures have received little consideration.

The shock-like syndrome, which may occur in severe malaria, is considered by this writer to be at least partially due to a deficiency of sodium chloride in the presence of dehydration and toxemia. This impression was gained from observations made while having occasion to treat a fairly large number of these patients during the recent war. Kean and Taylor[3] presented evidence to show that algid malaria is probably due to the development of medical shock. The observations of the writer concur in this. The similarity of this apparent syndrome of vasomotor collapse to that of severe heat prostration prompted an investigation of the sodium chloride balance of malaria patients. The finding that chloride levels of the blood tend to be low in the presence of evident dehydration has seemed to justify replacement of these vitally needed substances immediately when the first prodromal signs of shock appear. The early use of intravenous normal saline combined with five per cent glucose has been found to be of suf-

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ficient value that this measure is now frequently used in the treatment of malaria at Gorgas Hospital, Panama Canal Zone.

The following case report illustrates the therapeutic indications under discussion:

A 24-year-old white soldier was admitted to the hospital with complaints of fever, chills, backache and deafness. His first chill had occurred two days previously. He had been exposed to mosquitoes recently but denied having had malaria before. Malaria having been diagnosed at a local station hospital, he had received approximately 200 grains of quinine over two days. He was vomiting on admission and was semi-stuporous between paroxysms of nausea. A complete history was obtained with difficulty. Physical examination revealed oral temperature 103.2° F., pulse 108, respiration 24, dusky facies, dry skin and tongue, mildly injected throat, spleen palpable and tender, and blood pressure 100/60. The rest of the physical examination was not remarkable. Thick and thin blood smears showed both estivo-autumnal and tertian malarial parasites with 3 per cent of red cells parasitized. Blood count and hemoglobin were within normal limits. The patient continued to vomit, being unable to retain fluids or medication by mouth. Within a short time his dusky appearance had changed to pallor. His pulse had increased in rate and was of poor volume. Recheck blood pressure was 90/60. An intravenous infusion of 1,000 c. c. normal saline with 5 per cent glucose was prepared. As the needle was inserted 10 c. c. of blood was withdrawn into potassium oxalate for chloride determination. At the start of the infusion the patient showed obvious signs of impending shock. Before half of the infusion was completed he looked much better and his pulse volume had improved appreciably. On completion of the infusion his blood pressure was 120/60, he was able to converse freely, and his oral temperature was 100.4° F.; his pallor was replaced by almost normal color. A half hour later he was able to retain oral quinine and water. Seven hours later another 1,000 c. c. infusion was given. The next day his maximum elevation of temperature was 100.8° F. The balance of his convalescence was uneventful. The laboratory reported a blood chloride level of 374 mg. per cent.

The accompanying graph illustrates the results of an investigation of the whole blood chloride levels obtained on malaria cases of varying severity. The majority of these patients were those who seemed to present indications clinically for sodium chloride and fluid replacement. In all except two the blood sample was taken just prior to starting the intravenous infusion. These two were patients not on the writer's service. From the hospital record one who showed a blood level of 525 mg. per cent also did not have any clinical evidence of shock; his blood hematocrit value was 40 and blood pressure 120/80. The other patient had been given saline-glucose shortly after admission and the blood sample taken two days later showed 488 mg. per cent chlorides. The laboratory method for chloride determination was that of Volhard as applied to the Folin Wu filtrate of whole oxalated blood. This is a total chlorine determination but for practical purposes the value is reported as sodium chloride.

For the purpose of comparison of values obtained in malaria with those obtained in other conditions by the same method of determination used in our laboratory, eighteen values were obtained from laboratory and hospital records. Conditions were chosen in which evidence of chloride depletion might be expected. These included cases of pneumonia, pulmonary tuberculosis, acute disseminated lupus erythematosis, infantile vomiting with diarrhea, chronic dysentery, postoperative vomiting, acute rheumatic fever, peptic ulcer with vomiting and chronic bronchitis with marked sputum production. The normal range was considered to be 450 to 500 mg. per cent.

Urinary chloride excretion was measured in only two cases. One of these with a chloride blood level of 448 mg. per cent excreted 2.70 grams in 850 c. c. urine volume per 24 hours and the other excreted 4.89 grams in 740 c. c. per 24 hours with a blood level of 486 mg. per cent. Excretion of 15 grams of chlorides in 24 hours is considered normal in health.

Serum sodium determinations made on four other cases of malaria were found to be 275, 269, 284 and 294 mg. per cent. Cantarow and Trumper[2] place the average normal value at 330 mg. per cent. Serum potassium values obtained on the same patients were found to be 15.2, 11.3, 14.3, and 15.8 mg. per cent respectively. The average normal value for serum potassium is 19 mg. per cent.[2]

DISCUSSION

Warren *et alii*,[9] in discussing shock in acute infections, stress the fact that regardless of the cause of shock, it occurs as the result of a disparity of circulating blood volume and the size of the vascular bed. Other workers, notably Scudder,[7] who have made exhaustive studies of the general problem of shock, have stressed the

importance of a disturbance of the electrolyte balance. There exists a fairly complete agreement on the part of physiologists that the importance of sodium to the animal organism lies in its ability to activate and maintain a normal osmotic equilibrium in protoplasm. It is thus intimately concerned with the metabolism of water and the physico-colloid relationships in the extra and intracellular fluids of the body. Sodium is also considered to activate and stabilize the function of the vasomotor nervous mechanism. Here it acts as a physiologic antagonist of potassium.

The pathogenesis of shock in algid malaria may conceivably be initiated by abrupt release of malarial parasite proteins. This is conducive to an anaphylactic type of reaction. The shock reaction is further assisted by the intermittent hyper-pyrexia which tends to exhaust the vasomotor nervous mechanism. Excessive diaphoresis causes loss of sodium chloride. If vomiting is present this causes chloride loss. In fevers, for example, pneumonia, there is a primary chloride loss by the urinary route. As a deficit develops in the body it is indicated by decreased urinary chloride excretion. Sanchez-Vegas and Collins[6] stressed the value of urinary chloride determinations to evaluate sodium chloride deficit. They maintained that fluid and sodium chloride balance were not considered to be present until the patient was excreting in a 24-hour period at least 1,500 c. c. of urine, having a normal specific gravity and containing at least 5 grams of sodium chloride. The upper limit of normal by their method (Volhard-Hardy) was given at 10 grams per 24 hours.

Another consideration regarding the abnormal physiology of shock is the occurrence of an equalization of the normal disparity between plasma and cellular electrolytes.[7] Zwemer *et alii*[10] noted increases in serum potassium in monkey and human malaria. They felt that erythrocyte destruction during the chill could not account for all the potassium increase, inferring that part might be released from the body cells in general. This finding was not confirmed by the four determinations reported in the previous paragraphs but on the contrary the potassium values were subnormal.

It has been the practice of many to rely too much upon antipyretic drugs to combat the febrile exacerbations of malaria. This is definitely to be condemned. Phenacetin and closely related coal tar drugs are to be avoided because they depress the vasomotor nervous mechanism, provoking and prolonging diaphoresis. Hydrotherapy, the use of ice bags, and especially the administration of moderately cool saline-glucose intravenously are recommended as preferable alternatives. The addition of five per cent glucose to the normal saline furnishes a quickly available nutritive material much needed by the tissues exhausted by the increased metabolism of fever. Vitally needed sodium chloride in water is supplied. Circulating toxins or anaphylactogens are diluted. Urinary excretion is facilitated. Isotonic glucose alone was tried in two cases and it was observed that the progress of early signs of shock was not halted. The substitution of saline-glucose resulted in a prompt improvement. Atchley and Loeb[1] have emphasized the value of saline replacement therapy in dehydration and medical shock. Langer and other workers are quoted by Kolmer[4] as having found that sodium chloride, in amounts of 0.8 grams per kilogram body weight, given to lower animals would serve to prevent anaphylactic shock. Observations of Sicard and Parof[8] upon the use of sodium carbonate as a prophylactic agent against anaphylactic shock, would suggest the probable value of the sodium ion *per se*. Sodium lactate given orally has also been used in the shock syndrome of diabetes mellitus with some degree of success.

McDonald,[5] in a general consideration of parenteral fluid therapy, points out that whole blood sodium chloride estimations are of relatively little value because the chloride ion level varies considerably with the changes of the acid-base balance. It is granted, in agreement with Sanchez-Vegas and Collins,[6] that total urinary chloride excretion furnishes a better evaluation of salt deficit. The writer feels, however, that the findings in this study indicate to some extent a tendency to salt deficit in malaria. Certainly the therapeutic results of saline-glucose administration are excellent.

Routine laboratory chloride determinations are not considered necessary as the approaching syndrome of shock is self-evident. Hemoconcen-

tration is indicated in severe cases by increased hematocrit values. When the characteristically dusky color of the patient is observed to change to pallor, a delirium changing to apathy, a falling blood pressure and increasing pulse rate alter the clinical picture, this patient should have sodium chloride and fluid replacement. Once the syndrome of shock is definitely established it is recommended that plasma administration is the measure of choice to halt its progress. This supplies both electrolytes and balanced colloidal materials. The possible subsequent complications of plasma administration, for example, jaundice, as well as the expense involved, do not justify its use prophylactically.

SUMMARY

The shock-like syndrome which may occur in severe malaria, is considered by this writer to be at least partially due to deficiency of sodium chloride in the presence of dehydration and toxemia. It is suggested that the shock may be of anaphylactoid nature, becoming progressive because of sodium deficit. Evidence is presented, based upon whole blood chloride values, obtained in eighteen cases of malaria manifesting varying degrees of severity. Of the eighteen patients studied sixteen showed low normal and subnormal values. Urinary chloride excretion in twenty-fours was checked in only two of these patients. These values were also subnormal. Serum sodium and serum potassium values were subnormal in four other patients. Routine laboratory chloride determinations are not considered necessary as a guide to intelligent therapy since the progressive syndrome of shock is self-evident. Experience of the writer in the early administration of intravenous normal saline combined with five per cent glucose has seemed to justify its continued use. Glucose solution alone has not been found effective. The probable importance of the sodium ion *per se* in vasomotor and protoplasmic colloid stabilization is suggested.

The use of antipyretic drugs, especially phenacetin, to combat hyperpyrexia is to be condemned because of their tendency to depress the vasomotor nervous mechanism, provoking and prolonging excessive diaphoresis. As preferable alternatives the writer recommends administration of moderately cool intravenous normal saline with five per cent glucose, ice bags, and other forms of hydrotherapy. Once the syndrome of shock is definitely established blood plasma administration is recommended.

A case report has been presented in which the patient manifested signs of progressive shock and showed a whole blood chloride level of 374 mg. per cent. His condition promptly improved after administration of saline-glucose intravenously.

The writer wishes to acknowledge the technical assistance of James E. Jacob, Chemist at the Board of Health Laboratory, Gorgas Hospital.

WHOLE BLOOD CHLORIDES

MG Per Cent		
600		
590		Y
580		
570		
560		
550		YY
540		YY
530	X	YY
520		Y
510		YY
500		YYYY
490	X	Y
480		Y
470		Y
460	XXXXXX	
450	XXXX	Y
440	XXX	
430	X	
420		
410		
400	X	
390		
380	X	
370		

Fig. 1

Eighteen determinations, malaria cases (X), and eighteen determinations made by the same method in other conditions (Y) for comparison. Note tendency of malaria values to be low normals or sub-normals. All malaria cases confirmed by smears.

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THE RH-PROTECTIVE FACTOR IN CONGENITAL HEMOLYTIC DISEASE (ERYTHROBLASTOSIS FETALIS)*

By Allan Bloxsom, M.D.
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The existence of an anti-Rh antigen-antibody reaction factor was suggested[1] after an infant with hemolytic disease of the newborn (erythroblastosis fetalis) accidentally received a massive transfusion of Rh-negative blood and made a complete recovery. The demonstration of this factor was reported later.[2] Sufficient clinical and laboratory data have accumulated since to warrant this additional report on an inhibitory Rh-reaction agent which appears from the paralleling clinical and laboratory evidence to be a natural protective factor present in the blood of many Rh-negative individuals.

TECHNIC FOR TESTING FOR RH-PROTECTIVE FACTOR

Reagents.—Pooled sera (Rh +) of each of the four principal groups, AB, A, B, and O. Pooled cells (Rh +) of each of the four principal groups, AB, A, B, and O. Anti-Rh serum (our preference is the lyophilized serum obtained from the Buchanan Blood Serum and Plasma Center, Dallas, Texas), which is resuspended in 0.9 per cent NaCl solution (normal saline).

Cell Suspension.—Wash pooled clots of specific type until a heavy suspension of cells is obtained (use saline or Rh + serum). Centrifuge until cells are loosely packed. If there is any hemolysis, pour off supernatent fluid. However, if cells are so fragile that a second washing is necessary, they cannot be used. Resuspend cells in type specific Rh+ serum (pooled), making a 2-3 per cent suspension. Use one drop (from a 1 ml. pipette) into each tube of series, both tests and controls.

Blood for Testing.—Is obtained by venipuncture and placed in a sterile tube. No anticoagulant is used. Blood is allowed to clot. The clear serum is used for the test. The cells are checked for type and Rh factor.

Technic.—A series of ten Kahn size tubes is set up for each serum to be tested and another series of the tubes is set up for each control (a control is set up for each type of blood to be tested; that is, if there are types A and O in the sera to be tested, a control is set up for each). Like series of tubes are set up to check for iso-agglutinins in each serum to be tested. (In case of donors, the single tube test for iso-agglutinins is satisfactory when there is no history of transfusion or pregnancy.)

For Anti-Rh Antigen-Antibody Reaction Factor.

Tube	1	2	3	4	5	6	7	8	9	10
Unknown Rh-serum	0.15 c.c.	0.1 c.c.	0.1 c.c.	0.1 c.c.	0.1 c.c.	0.1 c.c.	0.1 c.c.	0.1 c.c.	0.1 c.c.	0.1 c.c.
Anti-Rh-Serum	0.05 c.c.									

(Mix and transfer 0.1 c. c. to tube 2. Mix and transfer 0.1 c. c. of tube 2 to tube 3, and so on throughout the series, this making the dilutions 1-4, 1-8, 1-16, 1-32, 1-64, 1-128, 1-256, 1-512, 1-1024, 1-2048).

Cell suspension as described above. Add 1 drop from 1 ml. pipette to each tube.

For Control	1	2	3	4	5	6	7	8	9	10
Rh + Serum	0.15 c.c.	0.1 c.c.	0.1 c.c.	0.1 c.c.	0.1 c.c.	0.1 c.c.	0.1 c.c.	0.1 c.c.	0.1 c.c.	0.1 c.c.

(Group specific)

Anti-Rh-serum 0.05 c. c. (Mix and transfer as above, to successive tubes). Cell suspension as described above. Add 1 drop from 1 ml. pipette to each tube.

Test for Iso-Agglutinins.—Set up series of tubes as for the control, using type specific pooled serum, but use 0.05 c. c. of serum to be tested instead of the commercial anti-Rh serum in the first tube. Proceed as in other series of tests.

Allow to stand at room temperature over night or incubate in 37° waterbath for 45 minutes. If room temperature drops as much as 15° below 37°, during the over night incubation period, place racks of tubes in waterbath for 15 minutes before centrifuging.

Centrifuge tubes at approximately 2,500 r.p.m. for 4-5 minutes. Read promptly. Tilt tube gently (any rough shaking of tube will completely mask a ± reaction.) Read before a frosted light (Kahn or microscope lights are satisfactory).

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Readings are: + (large, distinct aggregations of cells, with no outflow of single cells); ± (smaller aggregations of cells, with some dispersion of cells); — (no aggregation of cells).

If reading is a weak ±, reading may be facilitated by noting aggregate at bottom of the tube. ± shows a rough, irregular edged circle, while — shows a smooth circle with single cells flowing from the sides.

STUDIES

Twelve Rh-negative male donors who have received no transfusions have been tested for an anti-Rh antigen-antibody reaction factor in their blood sera. The results of these tests are shown in *Table 1.*

As a control, AB sera from Rh-positive male donors were used as the diluent. The results are listed at the bottom of *Table 1.*

The following data have accumulated on studies to determine the clinical significance of this anti-Rh antigen-antibody reaction factor.

First.—The lack of titers of the anti-Rh antigen-antibody reaction factors in the bloods of an infant dying of erythroblastosis fetalis (icterus gravis) at two days of age, a mother delivered of a stillborn erythroblastotic infant, and a mother whose infant died of erythroblastosis fetalis at three days of age, and in whom trouble was predicted, is shown in *Table 2.*

Second.—The titers of the anti-Rh antigen-antibody reaction factors in several infants and

Agglutinations of Rh-Positive Blood Cells with Anti-Rh Testing Serum Diluted with Serum of Rh-Negative Male Blood Donors

Donor	Type	1-4	1-8	1-16	1-32	1-64	1-128	1-256	1-512	1-1024	1-2048	1-4096
Wr.	A	±	±	—	—	—	—	—	—	—	—	—
Li.	A	+	+	+	±	±	±	±	±	±	—	—
St.	A	+	+	±	±	±	±	—	—	—	—	—
Mi.	O	+	+	+	±	±	±	±	±	—	—	—
Ba.	B	+	+	+	+	+	±	±	±	±	±	—
Ro.	AB	±	±	±	±	±	±	—	—	—	—	—
Lo.	AB	+	+	±	±	±	—	—	—	—	—	—
Na.	B	+	+	+	+	±	±	±	±	±	—	—
McDo.	O	±	±	±	—	—	—	—	—	—	—	—
Sc.	A	+	+	+	±	±	±	±	±	±	±	—
Bl.	A	+	+	+	±	±	±	±	±	±	—	—
Mu.	B	±	±	±	±	±	±	±	±	±	±	—
Control (Mixture of several Rh-positive blood donors.)	AB	+	+	+	+	+	+	+	±	±	±	±

Table 1

Agglutinations of Rh-Positive Blood Cells with Anti-Rh Testing Serum Diluted with Serum of Rh-Negative Mothers and Rh-Positive Infant, Infants Dying of Congenital Hemolytic Disease

Infant	1-4	1-8	1-16	1-32	1-64	1-128	1-256	1-512	1-1024	1-2048	1-4096
G.*	+	+	+	+	+	+	+	+	+	±	—
B. (serum from mother, infant macerated)	+	+	+	+	+	+	+				
M. (serum from mother, infant died two days after delivery)	+	+	+	+	+	+	+				

(*Titer of Anti-Rh testing serum for infant G had a titer of 1-4096, whereas, for infants B and M only a titer of 1-256.)

Table 2

Agglutinations of Rh-Positive Blood Cells with Anti-Rh Testing Serum Diluted with Serum of Rh-Negative Mothers and Rh-Positive Infants, The Infants Being Protected Against Congenital Hemolytic Disease.

Case*	1-4	1-8	1-16	1-32	1-64	1-128	1-256	1-512	1-1024	1-2048	1-4096
H. (infant)	+	+	±	±	—	—	—	—	—	—	—
(4) (mother)	+	+	+	±	—	—	—	—	—	—	—
R. (infant)	+	+	+	+	±	—	—	—	—	—	—
(1) (mother)	±	±	±	±	±	—	—	—	—	—	—
D. (infant)	+	+	+	+	+	±	—	—	—	—	—
(3) (mother)	±	±	±	±	±	—	—	—	—	—	—
P. (infant)	Insuff.										
(1) (mother)	+	+	+	±	—	—	—	—	—	—	—
Hl (infant)	Insuff.										
(1) (mother)	+	+	+	±	±	±	±	±	±	±	—
Ar. (infant)	+	+	±	±	±	—	—	—	—	—	—
(3) (mother)	+	+	+	±	±	—	—	—	—	—	—
Gr. (infant)	+	+	+	+	±	±	±	±	—	—	—
(2) (mother)	+	+	+	+	±	±	±	±	—	—	—

(*Titer of anti-Rh testing serum used for cases H, R, and D was 1-256. For cases P, Hl, Ar, and Gr 1-1024.)

Table 3

mothers, the infants being protected against erythroblastosis fetalis are shown in *Table 3*.

Third.—The titers of the anti-Rh antigen-antibody reaction factors in a few Rh-negative mothers and a few delivered Rh-positive infants, together with predictions as to the undelivered infants, are shown in *Table 4*.

COMMENT

With the exception of one Rh-negative male donor (Barzilla), all the Rh-negative male donors tested had a high titer of inhibition of the Rh-antigen-antibody reaction, some being higher than others. This one donor has given thirty-five transfusions. It is interesting to speculate upon the possible loss of a natural protective mechanism through numerous transfusions, as well as the possible loss of this inhibitory mechanism through repeated pregnancies. Such a natural using up of this inhibitory factor in repeated pregnancies with little replacement is seen apparently in a few mothers. The opportunity has not presented itself as yet to determine the inhibitory factor titers in succeeding pregnancies. Apparently it does vary, and can increase as well as decrease, for mothers have lost previous infants with erythroblastosis fetalis, and have been delivered later of normal infants who have received adequate protection.

All of the infants delivered upon whom inhibitory factors in the mother or in them have been only in high dilutions above 1-256 have not survived. The infants whose mothers, or who themselves, have had an anti-Rh reaction inhibition starting above dilutions of 1-16 and below 1-128 have survived.

The paralleling clinical and laboratory evidence with regard to the Rh inhibitory factor suggest that such a substance is a natural protective factor against the Rh antigen-antibody reaction. It is therefore proposed that the term Rh-protective factor denotes the Rh-inhibitory factor for the Rh antigen-antibody reaction.

The outcome of several pregnancies has been predicted with regard to the effect of maternal anti-Rh agglutinins on the blood of the fetus, and the titer of the anti-Rh antigen-antibody reaction factor. These predictions so far have followed the laboratory findings. It remains to be seen on a larger number of laboratory findings and predictions, whether this test for the inhibition of the Rh reaction will provide a useful means for prevention and treatment of erythroblastosis fetalis in the hands of the clinician.

Agglutinations of Rh-Positive Blood Cells with Anti-Rh Testing Serum Diluted with the Serum of Rh-Negative Pregnant Women (Husbands Rh-Positive) Together with the Anti-Rh Agglutin in Titers with Prediction as to Outcome of Pregnancy in those Women

Patient	Para in ()	Titers of inhibition of Rh reaction using Rh testing serum											Titers of Rh agglutinins							Prediction as to outcome of pregnancy
		1-4	1-8	1-16	1-32	1-64	1-128	1-256	1-512	1-1024	1-2048	1-4096	1-4	1-8	1-16	1-32	1-64	1-128	1-256	1-512	
Harkins	(4)	+	±	±	—	—	—	—	—	—	—	—	+	+	—	—	—	—	—	—	—Not predicted. Infant normal.
Meier	(6)	+	+	+	+	+	+	+	+	—	—	—	+	+	+	+	—	—	—		—Predicted infant would have cong. hem. disease. Infant died second day of cong. hem. disease.
Grubbs	(2)	+	+	+	+	±	±	±	±	±	—	—	+	+	+	+	+	±	±		—Predicted infant was in danger. Infant had to have transfusion immediately after birth.
Coulson†	(2)	+	+	+	+	+	+	±	±	±	±	—	+	+	+	±	±	±	±	±	Predicted infant in danger. Infant delivered with cong. hem. disease. Transfused at once.

(*The titer of the Rh testing serum used in the first case was 1-256, and after that was 1-2048).
†The case report of Coulson will be reported in full, as this is the first patient who has received a selected transfusion in an effort to obtain a viable infant.

Table 4

If after a larger group of predictions as to the future status of the infant *in utero* have been made successfully, then it may be advisable to give certain mothers having insufficient anti-Rh protective factor, serum from suitable donors in an attempt to attenuate or prevent Rh-reaction *in utero*.

It is apparent now that donors having Rh-negative blood should be tested for their Rh-protective factor (anti-Rh antigen-antibody reaction factor) to determine those most useful in the treatment and possible prevention of hemolytic disease of the newborn (erythroblastosis fetalis).

CONCLUSIONS

(1) Titers of an anti-Rh antigen-antibody reaction factor (Rh-protective factor from parallel laboratory and clinical findings) in infants and mothers starting in dilution of 1-256 or above, using an anti-Rh testing serum with a titer of 1-4096, have signified the development of erythroblastosis fetalis and eventual death.

(2) Titers of an anti-Rh antigen-antibody reaction factor (Rh-protective factor from parallel laboratory and clinical findings) in infants and mothers starting in dilutions of 1-128 or below, using an anti-Rh testing serum with a titer of 1-4096, have resulted in protection for those infants.

(3) Prediction as to the outcome of pregnancy complicated by the presence of anti-Rh agglutinins and the giving of potent serum for the inhibition of the Rh-reaction hold promise of success.

(4) Titers of "Rh-protective factor" (anti-Rh antigen-antibody reaction factor) should be done on all Rh-negative donors, and only donors having a high titer of this factor should be used in transfusions for erythroblastosis fetalis.

The author wishes to express his indebtedness to the many obstetricians in Houston for their active cooperation in carrying out this study, and to Miss Rose Matthaei and Dr. A. H. Braden for their technical assistance.

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THE MANAGEMENT OF PIGMENTED NEVI AND MALIGNANT MELANOMAS*

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The malignant melanoma, or as it is more conveniently called, the melanoma, is the most malignant and dangerous of all accessible cancers. A paradox to this statement is the amazing fact that the great majority of these so-called black cancers are preventable through early and appropriate treatment of the precursory lesion, the common pigmented mole or nevus.

In past years, considerable argument existed concerning the cells of origin of the melanoma, it being contended that some of them were of strictly epithelial character, and others were of mesoblastic development. Accordingly, they were referred to, respectively, as "melanocarcinoma" and "melanosarcoma." This arbitrary distinction of types was based not upon the methods of behavior, such as the routes of dissemination of these tumors, nor upon a careful study of the histogenesis of the particular cells of origin, but rather upon the morphologic features of the cells comprising these melanomas. Pierre Masson has clearly demonstrated that the neval cell and its malignant derivative, the melanoma cell, have their origin in relationship to the complex tactile end organ apparatus. In this sense, these tumors are derivatives of the peripheral nervous system and are neuro-ectodermal in origin. The pigmented moles or neuro-nevi and the melanomas may originate in the corium, and in some instances, they develop intra-epidermally, apparently in close relationship with the tactile and organ apparatus of Merkel-Ranvier. As these tumors develop, the differentiation which they undergo may proceed both functionally and anatomically. The cell is melanoblastic, and the malignant melanoma, therefore, is usually darkly pigmented as the tumors commonly possess the property of avidly withdrawing tyrosin from the blood stream and elaborating the complex chemical or chromagen, which is converted into the visible pigment

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*From the Mixed Tumor Service of the Memorial Hospital for Cancer and Allied Diseases, New York, New York.

through the activities of enzymes in the cytoplasm of the melanoma cell. Occasionally, the melanoma cells may be so actively reproductive, that is to say, expending so much of their energy in cell division, that the formation of pigment does not occur, and the tumors may appear to be non-pigmented. The converting enzyme, however, is present in the cytoplasm and can be recognized by the well-known dioxyphenylalanine reaction, commonly referred to as the dopa reaction. Anatomically, the nevi and melanomas sometimes differentiate to form abortive, bizarre forms of end organ apparatus, such as peculiar corpuscular arrangement of the cells simulating Meissnerian corpuscles. One does not usually see these structures in the highly malignant, rapidly growing, anaplastic melanomas.

Influence of Race and Complexion.—Pigmented nevi and melanomas are not commonly found in the darker races, particularly in the Negroes and Mongols. The Negro is singularly free from errors in the distribution of pigmented cells or neoplastic groups of such cells. The melanoma occasionally is seen in the Negro, and when found, it occurs most often in such locations as the sole of the foot, the nail bed, and the oral mucosa, regions which are not ordinarily deeply pigmented. With due consideration for the frequency of different complexions in racial types, it may be stated arbitrarily that malignant melanomas occur relatively more frequently in blond individuals, particularly those persons who have extremely pale skin, often translucent and of soft texture, and including those of sandy complexion who may freckle easily but do not tan well or heavily on exposure to sunlight. Such persons do not seem to have a well-developed resistance to the growth of pigmented tumor cells.

The incidence of pigmented neuro-nevi or moles in American population is very high, whereas the incidence of malignant melanoma is remarkably low, it being a relatively rare form of cancer. For several years, I plotted the incidence and distribution of pigmented moles among students, and in summary, may say that the average individual has approximately twenty visible pigmented moles by adulthood. Some persons have as many as a hundred such pigmented nevi, and others possess only two or three, but it may be accepted as a dictum that every member of the white race has at least one or more moles on his body, and *ipso facto* is potentially subject to the development of malignant melanoma. It is impossible to present any statistical data governing the frequency with which pigmented nevi undergo malignant degeneration into melanomas.

The regional distribution of pigmented nevi and melanomas in the skin is not exactly the same. Both tumors occur with considerable frequency on the face and neck, and with equal frequency in the skin of the trunk. Pigmented nevi are not commonly found on the feet and on the genitals, but the proportion of melanomas in these specific locations is relatively high. The proper inference from these facts would suggest that any nevus occurring on the feet or on the genitals would be particularly dangerous, and perhaps more likely to undergo malignant degeneration than the same tumor in other parts of the body. The reason for this higher incidence of transformation of nevi into melanomas might be explained on the basis of trauma by repeated irritation.

Prepubertal Melanoma: Influence of Hormone Stimulation.—The groups of neval cells constituting this congenital tumor may be in visible evidence at birth, particularly in the very large lesions, such as the bathing trunk nevi, or those which occupy a wide expanse of skin. The coloration of these tumors, however, seems to proceed after birth with exposure to light; in other words, the elaboration of the pigment does not seem to occur greatly *in utero*. By the time the child is a few years old, these tumors become much darker in color. Many of them do not increase in dimension except proportionately with the rate of the growth of the child. It is evident in studying the phenomena of the development of pigmented nevi, that many of them are not visible until after the onset of puberty. A child with a few scattered pigmented moles here and there may, in company with the endocrine changes attendant on the state of puberty, have the rather sudden development of numerous pigmented nevi over the skin of the face, trunk and extremities. It is assumed that these are not new growths, in the strict sense of

the word, but that the congenital misplacement of these cells may have been present but unrecognized until influenced by the hormonal factors which increased at this time. The nevi also undergo some remarkable pigmentary changes with the onset of puberty in that they become much more darkly pigmented and have a tendency to become elevated above the level of the surrounding skin.

There is an important type of pigmented nevus which bears such a close resemblance to malignant melanoma that it is not possible clinically to distinguish between the two. This nevus may be found in children from the ages of one to the time of puberty. Usually they are rather darkly pigmented, bluish, blue, black, or dark brown in color, smooth and well demarcated. When this tumor is excised in infancy or childhood and submitted to pathologists for diagnosis, they are frequently unable to say whether the neoplasm is benign or malignant, inasmuch as the histologic criteria, exclusive of invasion and permeation of vessels, are practically identical with the malignant variety of melanoma as encountered in adults. Even though the tumor has structurally the conformation of the true melanoma, it ordinarily does not behave as such until after puberty. Although there have been instances reported in the literature, our experience with now more than nine hundred cases of malignant melanoma has been that none of these melanotic tumors of infancy and childhood have metastasized to regional lymph nodes, although many of them have been labeled malignant melanoma by extremely competent pathologists. This fact is now so well recognized that our pathologists insist upon having clinical information available concerning the age of the individual, and whether or not evidences of approaching puberty exist. It would perhaps be very well if there were a universal acceptance of such a term as prepubertal melanoma to indicate this particular group of tumors, which resemble melanoma histologically but do not behave like them.

It is our belief, therefore, that the malignant melanoma in its derivation from the pigmented nevus, is a tumor closely related to the endocrine system and markedly influenced by the activity of the endocrines, notably the gonads, the suprarenal cortex, and perhaps the pars intermedia of the hypophysis. In keeping with this opinion, we have often observed malignant melanomas which occurred in adolescent girls and boys just after the age of puberty, and furthermore, we have commented upon the extremely rapid growth and wide dissemination of these tumors at this early age. Apropos of these statements concerning the stimulation of the tumor by hormones, it may be mentioned that we have never seen a patient who developed a malignant melanoma during pregnancy survive for any length of time. We have had quite a number of instances in which a pigmented nevus underwent malignant degeneration into melanoma during pregnancy or shortly thereafter, and when this occurred, the tumor grew with startling rapidity and was usually widely disseminated without control by surgical excision, however radical, or by any other method of treatment.

There has been considerable forensic interest in the reputed role of trauma in converting a benign pigmented neuro-nevus into a malignant melanoma. It does not seem possible that a single injury to normal skin can induce the onset of growth of a tumor so highly complicated as a neuro-nevus or a malignant melanoma. A report from Africa said that Sudanese natives have been found to have numerous malignant melanomas developing upon the soles of the feet, attributed to injury from an irritating thorn which commonly becomes implanted in the soles. In America, accumulated case histories would seem to suggest that repeated chronic irritation of pre-existing moles could be a factor in inducing their change into the malignant variety. This is particularly true when moles are found upon regions subjected to frequent and constant pressure, such as on the neck, the arms, the groin, the feet, and the genitals.

It is not always possible to observe by clinical means the transformation of a pigmented nevus into a malignant melanoma. In some instances, the melanoma appears to originate *de novo* from an apparently normal skin, but knowing the highly complex feature of the neoplasm, we believe that a nevus may have been present even though of microscopic size. Other patients presented themselves with evidence of

metastasis to regional lymph nodes, yet a closely adjacent pigmented skin tumor may clinically appear to be perfectly innocuous. When such tumors are excised, the pathologist may detect that the tumor is a true malignant melanoma, although not grossly recognizable as such. In other instances, however, the malignant melanoma may be seen as a bluish, elevated or ulcerated nodule, superimposed upon the margin or part of the body of a long existent pigmented nevus. In these tumors, the entire nevus is not necessarily involved by the malignant transformation. When a pigmented mole that has long been quiescent undergoes certain changes, such as becoming more elevated, with increased pigmentation, or with ulceration, bleeding and localized discomfort or pain, it may indicate that the tumor is becoming malignant.

It is appropriate to comment at this time upon the erroneous belief of many laymen, and unfortunately, some physicians that one should never remove a pigmented mole unless it bothers the individual who has it. This is a most dangerous doctrine. When a pigmented nevus begins to bother the patient, it may mean that a melanoma has already developed. The physician may excise what he believes to be a benign mole, and will do this operation in a conservative fashion in the office without microscopic study of the specimen, only to be chagrined later to have the patient return with evidences of regional or distant dissemination. If a pigmented mole is completely removed during its benign state, it never recurs as melanoma. The local recurrence of a melanotic tumor, or the appearance of metastases in regional nodes or distant viscera after the conservative removal of the supposed benign nevus, indicates that the original tumor was already malignant but unrecognized as such at the time of the conservative excision. This offers a strong argument for the routine microscopic study of every pigmented mole that is excised.

In the treatment of pigmented nevi and malignant melanomas, surgical excision is the only appropriate method of treatment.[3] These tumors are notoriously radio-resistant, consequently, x-ray and radium therapy are of no avail in bringing about their control or cure. Many patients have lost their lives through injudicious use of these agents in an attempt to control malignant melanoma. Melanoma is as radioresistant as the skin which contains it, and we have observed in the past, actual fungation of actively growing melanoma in skin exhibiting the epidermicidal effect of great doses of x-rays and radium. Conservative electrodesiccation of pigmented moles is fraught with considerable hazard, for several reasons, namely: (1) the specimen is often destroyed and a biopsy is not always taken prior to the destruction of the tumor; (2) the electrodesiccation is too superficial and not wide enough to remove all of the neval cells; and (3) if a part of the tumor remains, after the electrocautery, the irritation of this procedure may induce it to grow more rapidly and even become malignant.

Once the diagnosis of malignant melanoma is made, the surgeon must perform an extremely wide surgical excision of the tumor and the skin which surrounds it. Cosmetic restoration is not so important as safety, which is afforded by wide and deep surgical excision. In the majority of instances, the removal of skin must be so great as to necessitate an immediate application of a skin graft. The excision should go so deeply that not only the skin, but the underlying fat and fascia overlying the muscles, should be removed in order to extirpate the adjoining lymphatics in the neighborhood of the melanoma.

Routes of Dissemination of Malignant Melanoma.—The best prognosis, of course, occurs when the malignant melanoma is widely excised by these methods, before metastasis has occurred. It is not always possible to detect metastases in the early stage, and to know by which of the vascular routes the cells will be disseminated. Those malignant melanomas that seem to metastasize by way of the regional lymphatics are still amenable to surgical treatment, but those melanomas which early enter the blood vascular system will spread through venous channels and these patients ultimately will develop visceral metastases and hence are incurable. It is, therefore, impossible ever to effect a cure for malignant melanomas which have undergone the accident of penetration into venous channels draining the skin in which the tumor is situated. The malignant melanoma differs from all other cancers in one important

respect, namely: that the metastases from this tumor will locate and grow in any tissue or organ. In a study of the natural history of most cancers, the pathologist and the clinician come to understand that certain cancers are prone to locate secondarily in various tissues which seem to favor the location and growth of metastases of their type. But in the case of malignant melanoma, the melanotic cells will grow in every organ of the body. Metastases even occur in the heart muscle. Making allowances for the relative frequencies of different types of cancer, it may be said that malignant melanoma metastasizes to the brain more frequently than any other histologic type of organ distribution.

It is a subject in itself to study the occurrence, the appearance and the behaviors of melanomas of certain regional types, for example: those occurring within the eye, the so-called ocular melanomas, which are quite favorable in that many of these patients will live for a great many years, or even be cured after exenteration of the orbit. A common phenomenon associated with ocular melanomas is the fact that when metastases do occur, they usually spread under pressure through the central vein of the retina, and the metastases almost invariably lodge in the liver, but may not grow for many years, even ten or twenty years after the eye has been removed. What factors are influential in permitting these metastatic melanoma cells in the liver to lie latent or dormant and inactive for this time has never been satisfactorily explained. The melanomas occurring in the nail bed or nail matrix are seldom recognized in their incipiency, but they constitute an extremely favorable type of tumor, because they are relatively slow growing, metastasize somewhat later than the usual type, and the patients will readily consent to an amputation of the digit.[1,2] Melanomas occurring on the genitals, on the other hand, are extremely malignant, and even those which are detected at the time when they are minute are seldom cured, even by such radical measures as a bilateral groin dissection and radical vulvectomy or radical penectomy, done in a single operative seance.[4]

The principle of treatment of malignant melanoma which we have championed has been so-called excision and dissection in continuity for primary and metastatic melanoma in regional lymph nodes.[5] This principle can be applied when the malignant melanoma is so situated in the skin as to be relatively closely adjacent to the first relay of lymph nodes. The principle includes the procedure of performing a wide elliptical removal of skin to include the primary melanoma, the skin intervening between the melanoma and the axilla or groin or neck, an excision of the skin of the lymph node-bearing region, together with a wide dissection of the underlying fat and fascia, down to and exposing the muscle over this area. The operation is completed by a radical dissection of the regional lymph nodes which may contain metastatic melanoma. The fascial dissection is much wider than the sacrifice of the skin. By this means, not only is the primary tumor removed and the first relay of metastases in regional nodes, but the intervening lymphatics as well. This measure should ensure to some extent the great tendency for metastases to develop in the intervening

PRIMARY SITE OF MELANOMA FROM 1917 TO 1946
The Memorial Hospital for Cancer and Allied Diseases, New York, N. Y.

Site		Per cent
Lower extremity		27.0
Exclusive of feet	12.7	
Feet, exclusive of nails	12.2	
Subungual	2.2	
Head and neck		23.1
Trunk		17.9
Upper extremity		13.7
Exclusive of hands	10.1	
Hands, exclusive of nails	2.3	
Subungual	1.2	
Eye		8.6
Vulva and vagina		3.6
Oro-nasal mucosa		2.6
Lip	0.6	
Gingivae	0.6	
Palate	0.4	
Paranasal sinuses	0.5	
Rectum and anus		1.5
Genitalia, male		0.4
Unknown primary site		1.5

Distribution according to site is based upon 851 cases, since the site was not stated in 11 of the 862 cases reviewed.

Table 1

tissues between the primary site and the regional lymph nodes. The application of this principle in the treatment of melanomas has been responsible for our greatest improvement in end-results. Unfortunately, the condition sometimes exists where the primary malignant melanoma is situated in the skin at a remote site from the regional lymph nodes, involved by metastases; for example, a melanoma on the sole of the foot with metastases in femoral and inguinal lymph nodes, or a melanoma occurring in the nail matrix on the hand with metastasis in axillary lymph nodes. With such an enormous intervening distance between the primary melanoma and the metastases in regional lymph nodes, it is not at all possible by any technical procedure, to remove both primary and metastatic foci with a dissection of all of the intervening lymphatics between the two sites. It is hazardous to permit any of the intervening lymphatics to remain, because with the dissemination of malignant melanoma by way of the myriad of lymphatic vessels, the accidental lodgment of the melanoma cells anywhere en route would lead inevitably to local recurrence in the arm or leg. In fact, this complication has occurred so frequently in patients, for example, having an amputation of the great toe with groin dissection, with metastases occurring subsequently in the skin and subcutaneous tissues of the intervening leg, that it was realized a more radical operation must be planned.

Although the patient and the physician might immediately consent to such a radical operation as hip joint disarticulation for a bone sarcoma of the femur, it has been difficult to secure consent for this operation in the case of a small melanoma on the ankle with metastases to regional lymph nodes, and yet the disease is as fatal as other types of cancer which have more frightening aspects. The proper procedure for a melanoma of the hands or feet with metastasis to axilla or groin, respectively, is an amputation of the entire extremity with dissection of regional lymph nodes.[6] Only by such measures can all of the intervening lymphatic network be removed, and with it the hazard of deposition of melanoma cells and local recurrence in the intervening tissues. In other words, in the lower extremities, the patient must undergo a hip joint disarticulation with a dissection of the deep lymph nodes in the groin, which would be done by splitting the inguinal ligament, lifting up the peritoneum intact, and dissecting the iliac lymph nodes from the bifurcation of the vessels

FIVE-YEAR END-RESULTS IN 595 CASES OF MELANOMA IN RELATION TO AGE GROUPS
(Includes all cases, operable, inoperable, and recurrent, in all stages of the disease)

Age period	Total cases	Per cent of five-year survivals
Prepuberty	10	100.0
Puberty through 24 years	22	5.3
25 through 39 years	145	8.2
40 through 59 years	250	9.6
60 years and over	168	10.0

Table 2

FIVE-YEAR END-RESULTS IN 595 CASES OF MELANOMA IN RELATION TO PRIMARY SITE OF TUMOR

Site	Number	Per cent
Lower extremity		
Leg, exclusive of feet	73	4.8
Feet, exclusive of nails	77	14.5
Subungual	9	11.0
Head and neck	138	8.8
Trunk	98	9.8
Upper extremity		
Arm, exclusive of hand	59	6.3
Hand, exclusive of nails	16	42.0
Subungual	9	11.0
Eye	58	12.8
Vulva and vagina		
Vagina	2	None
Vulva	23	4.5
Oro-nasal mucosa		
Lip (muco-cutaneous)	3	66.7
Gingivae	4	None
Palate	3	None
Paranasal sinuses	6	None
Rectum and anus	5	None
Genitalia, male	3	None
Unknown primary site	8	12.5

Over-all five-year survival rate, 9.7 per cent; no sex difference.

These end-results are based upon all patients applying to the Memorial Hospital with malignant melanomas in all stages of the disease including all the inoperable and recurrent cases.

Table 3

retroperitoneally down to and including the inguinal region. In the upper extremity, with a similar situation of malignant melanoma of the hand metastatic to axillary lymph nodes, the surgeon would perform an interscapulo-thoracic amputation, which is a removal of the scapula, the clavicle, and the entire upper extremity associated with a dissection of the lower cervical lymph nodes; in this operation, the axilla is removed, rather than dissected, and the surgeon has greater assurance of carrying the dissection superior to the upper limits of dissemination of the melanoma. The operation of interscapulo-thoracic amputation is relatively safe, as it has been done more than fifty times at the Memorial Hospital, without an operative death.

The end-results in the treatment of malignant melanoma by the adoption of these radical measures have greatly improved. In the past fifteen years, our percentage of patients who have survived five years without recurrence, that is to say, the so-called definitive cures, has increased 600 per cent, surely an improvement far greater than obtained with almost any other common variety of cancer. Its improvement can be attributed entirely to the adoption of the principles of radical surgical therapy as outlined in this manuscript. Even at best, however, the end-results are poor when compared with cancers of other locations. For example, the percentage of five-year survival for operable malignant melanomas without metastasis to regional lymph nodes is 18. The percentage of five-year survival for operable malignant melanomas metastatic to regional lymph nodes and treated by surgical means is 15.

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A HUGE CALCIFIED INTRACRANIAL OLIGODENDROGLIOMA*

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and
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Calcification, roentgenologically demonstrable, may occur in certain normal structures of the brain as well as in many intracranial lesions. In 59 per cent[1] of adults the pineal gland can be visualized in the midline on the antero-posterior view of the skull. The falx cerebri may show calcification in any of the membranes but it is most commonly found in the frontal region. The tentorium may be calcified and lastly the choroid plexuses which usually cast bilateral shadows.

Roentgenologically visible calcium occurs in many intracranial tumors. It is seen in 41 per cent[2] of the supraseller cysts and in 31 per cent[3] of the oligodendrogliomas; 7 per cent of the dermoids show it and occasionally an astrocytoma or a chordoma. The astroblastomas, spongioblastomas, neuroblastomas, three rapidly growing tumors, rarely reveal calcium roentgenologically. Calcification never occurs in the acoustic neuromas. Parallel streaking is noted in the benign venous tumors while the hemangioblastomas never calcify. Of the non-neoplastic conditions calcium is rarely seen in old hemorrhages or scars.

Excluding normal sites, calcium deposits usually indicate tumors. According to Dyke[1] the amount within a tumor varies from a mere fleck of pin-head size to that several centimeters in diameter. The pattern varies, being amorphous, finger-like or punctate.

Huge calcified intracranial tumors are rare; only a few cases were noted in the literature. Heuer and Dandy[4] reported two cases. The shadows in one measured 4 x 5 cm. and in the second case the shadow was 3 x 6 cm. O'Sullivan[5] reported several large intracranial calcifica-

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tions. Light's[6] case is probably the largest and very similar to ours. His tumor revealed, on roentgenogram of the skull, a huge, almost uniformly dense shadow measuring 7 x 7 cm. in the left frontal region. Its outline was jagged and irregular. Histologically it was an oligodendroglioma.

CASE REPORT

The patient, P. K., was a 52-year-old white male admitted to this hospital October 11, 1945, from another institution, for brain surgery. Since early 1944 he had shown a peculiar, silly laughter and a marked neglect of his personal appearance and although normally quick tempered and arrogant he had become most humble and childish. There were periods of melancholia and self pity and during these periods he appeared unable to handle himself properly, stumbled and limped when he tried to walk. He sometimes was nauseated and vomited for long periods of time.

Physical examination revealed a well developed male. The eyes reacted in a small arc to light and to accommodation. The fundi showed definite arteriosclerosis with many flame-shaped hemorrhages about the arterioles. Both discs were blurred, the left more than the right. There was diminution in the visual fields to the left side in both eyes. The remaining neurological examinations including the reflexes of the abdomen and extremities were essentially negative. Both the heart and lungs were normal and the blood pressure was 130/90.

A spinal tap revealed a clear fluid with 20 lymphocytes per c. mm.; protein 15 grams; Wassermann was negative; a colloidal gold curve of 232,100,000,000. The routine laboratory tests were negative.

Roentgenograms of the skull (*Figs. 1* and *2*) showed a large, oval, confluent, calcific mass in the right lower and lateral aspect of the partial lobe which measured 7½ x 4 x 4½ cm. Its margins were somewhat serrated suggesting conformity with the adjacent convolutional configurations. The sella tursica was normal. There was slight calcification in the falx cerebri which was seen to lie in the midline. There was no evidence of any pathology of the bones of the vault. On November 8, 1945, a craniotomy was performed by Dr. H. H. Kerr, consulting neurosurgeon, and a large calcified tumor was removed.

The specimen consisted of an irregular, stony, hard mass approximately 7.5 x 5 cm. Most of the mass was composed of a yellowish-white stony material, presumably calcium. Attached to the mass were soft, hemorrhagic fragments of tissue.

Sections from the outer soft tissue revealed a calcified tumor composed of approximated cells containing round uniform nuclei surrounded by a clear halo and characteristic of an oligodendroma. There were numerous blood vessels, some of which showed calcareous deposits in their walls. Hemorrhagic areas also were prominent. There was another section composed of bone outlined by osteoblasts and containing marrow that was loose and fibrous. On one surface was attached a loose fibrous tissue containing calcareous deposits and presumably representing parts of the tumor immediately adjacent to the skull without actual invasion.

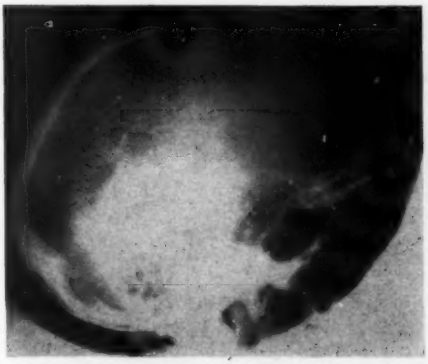

Fig. 1
Lateral roentgenogram of the skull showing a huge calcified oligodendroglioma.

Fig. 2
Antero-posterior roentgenogram of the skull showing a huge calcified oligodendroglioma.

His course was uneventful and he was discharged November 27, 1945, as symptom-free.

SUMMARY

Roentgenologically demonstrable calcium may occur in certain normal structures as well as in many intracranial tumors.

A huge calcified intracranial oligodendroglioma roentgenologically demonstrable is reported in a 52-year-old-male.

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CALCINOSIS*

A BRIEF REVIEW OF THE LITERATURE AND REPORT OF TWO CASES

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Calcinosis is an infrequent condition characterized by the deposition of calcium salts in the tissues. These may be (1) localized around joints, frequently bilaterally, in the skin and subcutaneous tissues, or (2) diffusely in the skin, subcutaneous tissue, muscles and tendons. To the first condition the term calcinosis circumscripta has been given, and to the second calcinosis universalis.

Steinitz[1] made the first comprehensive review of the literature on calcinosis in 1931. Of a total of 105 cases, he found 71 cases of calcinosis circumscripta and 34 cases of calcinosis universalis. By 1938 there had been 137 cases of calcinosis circumscripta alone, and 78 cases of calcinosis universalis.[2] Since then there have been numerous reports of cases of the disease with wide variation in apparent etiology and treatment. Calcinosis universalis has been found to occur predominantly in the first two decades of life, and is almost equal in the sexes, but slightly more frequent in females. Calcinosis circumscripta occurs in females in 85 per cent of the cases and with very few found earlier than the second decade.[3] There has been found no limitation of the disease as to race or locality. Two instances have been reported of some familial tendency. Duret[4] observed the disease in a brother and sister, and the mother of the patient described by Lereboullet and Lelong[5] was known to have a deposit in the arm.

Our knowledge of the etiology of the disease has increased little since it was first described in 1877.[6] Numerous theories have been suggested, but as yet no one theory seems acceptable. Bloxsom and Johnston[7] reported an infant with calcinosis universalis and it was their observation that the disease was due to a disturbance in the placenta or in the maternal calcium metabolism. Aisenberg[8] reported calcinosis in a child and considered an attack of malaria as a precipitating factor. Numerous reports emphasize trauma and infection as possible precursors of calcinosis, but conversely there are many other cases reported in which no contributory factors could be incriminated. Whereas many children with calcinosis gave histories of one or more childhood diseases prior to the onset, the evidence that these diseases had any direct bearing on the condition was inconclusive.

There are certain conditions which accompany calcinosis so frequently that their coexistence would seem to be more than coincidental. Scleroderma, sclerodactylia, and Raynaud's disease are associated frequently with calcinosis, particularly with calcinosis circumscripta. Forty per cent of the cases of the latter type also have scleroderma, whereas 32 per cent of the cases of calcinosis universalis show this disease.[2] Brody and Bellin[9] reporting two cases concluded that vasomotor spasm was the basis for both diseases and that the pathologic changes were determined by the rate of tissue destruction resulting from the occlusion of the circulation.

Parathyroid gland disturbances have been considered by some investigators to be a causative

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factor in the pathogenesis of calcinosis, but calcium and phosphorus studies in almost all reported cases have not borne this out. Bauer, Marble and Bennett[10] did extensive chemical, histologic, and metabolic studies on a patient reported by Wilens and Derby.[11] It was their observation that in spite of normal blood values there was a marked tendency to retain absorbed calcium and phosphorus. They suggested that the basis of the disorder is abnormal calcium and phosphorus metabolism, and that the increased retention is the result of local cellular conditions.

Chemical studies of both the blood and urine have failed to reveal pertinent information which might be of any significance. Moggi[12] reported a case with hypercholesteremia, but this has never been duplicated by others. The hemoglobin content of the blood has shown wide variation from normal to low values. Urinalyses reported have been of no significance.

Surgical removal and analysis of the subcutaneous deposits found in calcinosis show them to consist chiefly of calcium phosphate and calcium carbonate. Quantitatively they contain a comparable ratio of calcium (less that in the form of calcium carbonate) to phosphorus (1.87) as the theoretical ratio for these substances in normal bone (1.94) (Bauer, Marble and Bennett).[10] Microscopic sections of the affected areas usually show the deposition to have taken place in fat or subcutaneous tissue, and in most cases there is no evidence of necrosis or degeneration of these tissues.

Case 1.—A nine-year-old white boy (*Fig. 1*) was admitted to Duke Hospital with a history of having had a "drawing" of the knees with swelling and fever two years before admission. At about the same time an erythematous maculo-papular rash developed over the face and neck. Because of the findings a diagnosis of Still's disease had been made at another hospital. Seven months before admission hard nodules developed in the loose tissues of the popliteal fossa, and shortly thereafter many more appeared in the dermal layers and deeper structures of the lower extremities.

On physical examination an elevated temperature of 38.8° C. was found. A diffuse scattering of hard nodules was found in the skin, subcutaneous tissues and deeper structures, most marked over the lower extremities. An erythematous maculo-papular rash was present over the head and neck. There was limitation of extension and flexion of both knees and both elbows. The spleen was palpable just below the left costal margin, and lymphadenopathy was generalized. The heart was beating rapidly, but was not enlarged and was without murmurs.

Laboratory findings were as follows: hemoglobin, 68 per cent; white blood count, 5,350; urinalysis showed a few white blood cells. The Wassermann reaction was negative. The phenolsulfonphthalein excretion test showed a total of 48 per cent in two hours. Analysis of the blood showed a non-protein nitrogen of 42 mg. per cent, plasma proteins 6.5 mg. per cent, blood calcium 10.2 mg. per cent, phosphorus 5.4 mg. per cent, and phosphatase 6.2 Bodansky units.

Fig. 1, Case 1
The deformity of the upper extremities followed an attack of Still's disease. The discolorations are in the areas of subcutaneous nodules.

No evidence of myocardial disease was found by electrocardiography. Roentgenograms showed marked amorphous calcifications throughout the lower abdomen (*Fig. 2*), pelvis and femoral regions. There were flecks of calcium in the soft tissues and muscles of the upper extremities, and diffuse calcification in the lower extremities (*Fig. 3*). Film of the abdomen showed a calculus in the right renal pelvis. Biopsy of a lesion from the right thigh showed extensive deposition of calcium in the fibrous and fatty tissue.

The patient was put on a ketogenic diet with a 3:1 ratio. Reexamination by x-ray and physical examination 10 weeks later showed an increase in the process.

Case 2.—A one-year-old female colored child was brought to Duke Hospital because of the presence of nodules under her arms. Four months before admission the patient had chickenpox, recovering quickly without apparent complication. A few days after recovery the mother found small nodules on the posterior surface of the left leg below the knee, and in two weeks they were found on the opposite leg. No further change was noted until two months before admission when nodules were found over the chest and arms.

History revealed that the mother received antiluetic therapy during pregnancy. The child had had three negative blood serum tests since birth.

Physical examination was positive only for numerous subcutaneous nodules found over both arms, shoulders, axillae, chest, and legs. Some were attached to deeper structures.

Laboratory studies showed a hemoglobin of 10.6 grams, with 9,500 leucocytes and 3,590,000 erythrocytes. The urine was normal. The Wassermann, Schick and tuberculin tests and sickle cell preparation were negative. The blood calcium was 9.3 mg. per cent, phosphorus 5.3 mg. per cent, phophatase 4.6 Bodansky units.

Roentgenograms showed extensive deposits of calcium in both the subcutaneous tissue and muscles and tendons of the arms and legs (*Figs. 4, 5*) and in the subcutaneous

Fig. 3, Case 1
There are calcific deposits in the subcutaneous tissues over the anterior aspects of both lower legs and in the muscles and tendons of the thighs.

Fig. 2, Case 1
Amorphous deposits of calcium extend throughout the pelvic and upper femoral regions.

Fig. 4, Case 2
Extensive deposition of calcium has taken place in both upper extremities.

tissues of the chest and abdomen (*Fig. 6*). A biopsy of one of these areas overlying the right biceps muscle was taken, and microscopically showed considerable necrosis of adipose tissues with deposition of calcium in these areas.

Fig. 5, Case 2
In the lower extremities the deposits are again predominantly on the anterior surface of the lower leg and posterior deep tissues of the upper leg (*Fig. 3*).

Fig. 6, Case 2
Calcification has occurred in both axillary regions.

The patient was discharged under the care of her local physician with oral glutamic acid.

There have been numerous methods used in the treatments of calcinosis including x-ray therapy, potassium iodide, ammonium chloride, sodium citrate, disodium phosphate, heliotherapy, electrophoresis, ketogenic diet and parathyroidectomy. For each type of treatment some benefit has been claimed; however, the mere existence of so impressive a list of treatments, attests to the fact that no one has had any consistent success therapeutically. Ramsdell[13] did hemithyroidectomy and parathyroidectomy on four cases with excellent results in one and improvement in three, but Byron and Michalover[14] failed to note improvement following similar treatment. The fact that spontaneous regressions have been reported[15] is significant, for this makes it difficult to evaluate any of the proposed methods of treatment. Only when uniformly beneficial results are demonstrated can the treatment be considered satisfactory.

SUMMARY

Two cases of calcinosis universalis are described, both occurring in children under 10 years of age. The disease is of interest to the pediatrician, radiologist, and general practitioner, primarily with respect to its recognition, for although over 100 cases have been studied and reported, both the diagnosis and etiology remain obscure. Pathological study of biopsy material from the above two cases showed no evidence of tissue necrosis in one, while in the second the calcium deposits were found in areas where considerable fat necrosis had taken place. In neither case was there any association with scleroderma, sclerodactylia, or Raynaud's disease.

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PILONIDAL SINUS: TREATMENT BY EVENTRATION*

A REPORT OF 618 CASES

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Incision, rather than excision, is the method of choice in treatment of sacrococcygeal cysts or pilonidal sinuses. This conviction is founded on pathologic study and surgical observation of more than 600 cases.

The nidus of ectoderm (*Figs. 1* and *2*), possessing all of the appendages of skin, even though quiescent, grows hair and secretes sebaceous and sudoriferous material. When asymptomatic it exists as a sacculation with adequate drainage. Following trauma, the ostium may close and with entrapment of the secreted products inflammation usually occurs. The lining epithelium thins under pressure of the growing abscess and is partially destroyed (*Fig. 3*).

When the abscess is drained by spontaneous rupture or by surgical intervention, there is a rapid subsidence of the acute process. The remaining epithelial cells regenerate to line the enlarged sinus which becomes surrounded by a thick layer of fibrocytes that forms as a barrier to the adjacent healthy tissue.

Repeated exacerbations depend entirely upon additional trauma and obstruction to drainage. The process extends by rupture of the scar-encased sac, the reformation of the epithelial lining and accumulation of additional scar.

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In treatment by excision, in order to assure complete removal of diseased parts, a generous amount of healthy tissue has to be sacrificed. The defect that remains can be healed by granulation or by some type of plastic repair. Healing by third intention gives the greatest assurance of eventual success although the convalescence may be long delayed and too frequently ends in a wide and painful scar that is adherent to the sacral fascia. Plastic closure has many advocates. The variety of the methods suggested indicates the insecurity of any one. The frequency of recurrences and protracted periods of healing brings to question the rationale of excision.

With the increasing knowledge of the subject, especially during the past five years, some investigators have attempted to treat pilonidal cysts and sinuses by marsupialization. Block[1] incises the tracts and destroys the membrane with Carnoy's* solution. Buie[2] advocates saucerization with removal of a major portion of the lateral walls and suturing the remaining membrane to the skin. Both report good results by their methods.

It seemed that somewhere between these two forms of treatment was a possible solution to the problem. If the inner lining of the cyst or its remains could assume the function of normal skin, a satisfactory end result would be obtained. Observation on exteriorizing this membrane in over 600 cases of pilonidal disease during the past six years has shown this to be true.

The average healing time was greatly reduced. Scarring was minimal and asymptomatic. Recurrences were infrequent.

Operative Procedure.—Following spinal anesthesia the patient is placed face downward with a pillow under the hips. The operative site is prepared with ether, soap and water, and a mercurial tincture. The buttocks are not strapped, nor are dyes used to outline the sinus cavity because of the questionable value of such procedures. The lesion is carefully palpated and all openings are probed to determine the extent and direction of the pathology. By means of a grooved director or sharp-pointed scissors inserted into the ostium, the sinus roof is opened through its entire length so that the inner mem-

*Glacial acetic acid 9.0, alcohol 95 per cent, 54.0 chloroform, 33.0 ferric chloride, 5.0 grams.

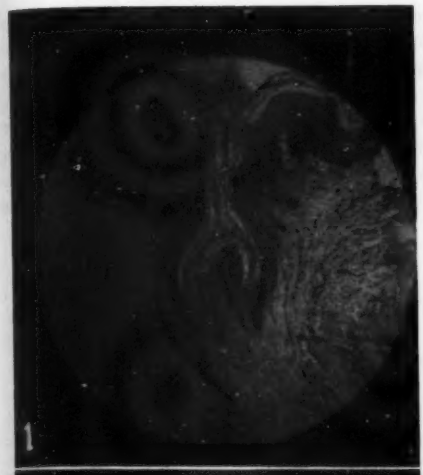

Fig. 1
Microphotograph of a superficial uninfected pilonidal sinus.

Fig. 2
Microphotograph showing deep, invagination of epithelium in an uninfected pilonidal sinus.

brane lies like cup in the wound. The necrotic contents of the cavity are wiped away. Depressions and dimplings on the cyst wall indicate secondary extensions. These, if present, require further exploration by probing. Superficial, secondary tracts of 4 mm. or less are left undisturbed; deeper ones, regardless of direction, are thoroughly exposed by incision. When the center cavity and radiating branches have been opened widely and cleansed, the severed margins of the lining epithelium and inflammatory base are sutured to the skin with cotton (*Figs 4* and *5*). No tissue is removed.

Carnoy's solution is applied to the cavity with a cotton applicator. Used in this manner, it does not seem to affect the healthy tissue nor does it destroy the membrane. Care is taken

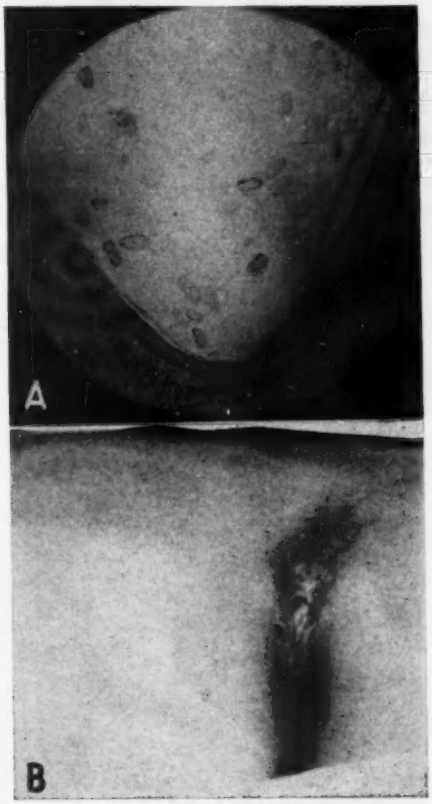

Fig. 3(A)
Epithelial lining thins under the pressure of infection and abscess formation.

Fig. 3(B)
Photograph of an acutely infected pilonidal sinus.

not to injure the wall but only to fix or coagulate the contents of the cyst. One per cent silver nitrate acts in a similar manner but with less effectiveness. Various mercurial tinctures have also been tried but do not work as well in acting as a hemostatic, in cleansing the cavity of cell debris and in shortening the healing time. Dry dressings are placed in the wound.

Anchoring the membrane as described seals off nearly all of the space between the skin and cyst lining. With the aid of the mildly escharotic solution, bleeding is quickly stopped. If the capacity of the cavity is measured at the time of operation and again at the first dressing, there will be a marked reduction. By establishing maximum drainage to the enclosed space, the compressed, inflammatory tissue surrounding

Fig. 4 (A and B)
The abscess has been widely incised and the membrane sutured to the skin followed by Carnoy's solution.

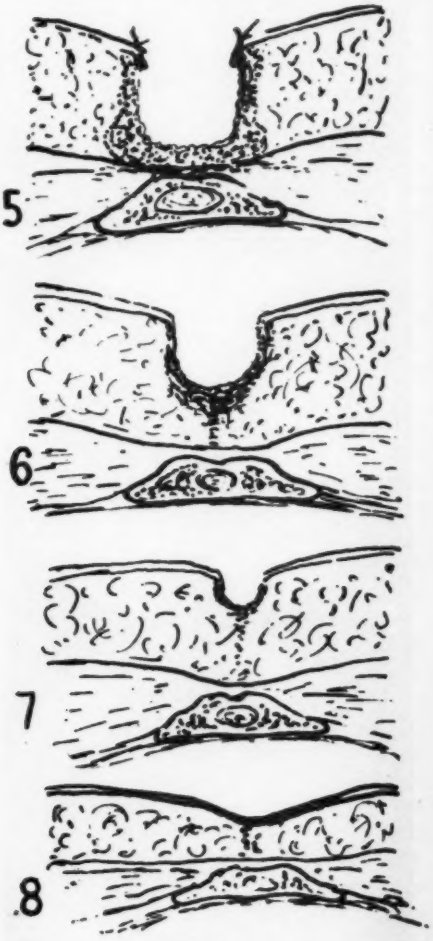

Fig. 5
Cross section showing abscess wall and compressed tissue.

Fig. 6
Lifting of inflammatory membrane from sacral fascia.

Fig. 7
Contraction of membrane and expulsion.

Fig. 8
Flat scar, freed sacral fascia, and good fat pad.

the lesion seemed to return to a more normal consistency (*Fig. 6*). As the size of the cavity lessens, the protecting inflammatory wall resolves and releases the parasacral tissue. The loose areolar tissue that had been forced aside by pressure of the abscess and extention of subsequent inflammation returns to a position that later permits free movement of the natal scar (*Fig. 7*).

Postoperative treatment consists of daily application of hydrogen peroxide and 5 per cent mercurochrome. A thin strip of fine mesh gauze kept in the wound and changed several times daily aids in keeping the lesion from macerating. Occasional application of 10 per cent silver nitrate will stimulate wound contraction. Patients are permitted out of bed on the first postoperative day. Bathing by shower is allowed after the third day. There are no diet restrictions nor interference with normal bowel habits. Pain is rare. Discomfort is reduced to a minimum and rarely requires medication. The sutures are removed on the fifth day.

Acute abscesses which previously required initial incision and drainage with subsequent excision of the contracted cyst are also treated by incision and eventration as a single stage procedure. If the pressure of the abscess was of short duration, the epithelium will not be excessively destroyed. The healed scar (*Fig. 8*) will show vestigial remains of sweat glands and grow laguna hairs.

Hospital care is terminated after the sutures have been removed. The remainder of the convalescence is spent in the reconditioning section or a return to light duty. Patients are instructed to bathe at least once daily and to keep a gauze wick in the wound at all times to prevent soilage of clothes. Twice weekly they return to the outpatient clinic where the wounds are treated, the surrounding hair shaved and the progress of healing noted.

The period of healing varies with the extent and duration of the disease. From this series of cases, certain facts have been determined. Acute infections heal most rapidly, some in as little as ten days. In the chronic or recurrent variety complete healing will be accomplished in three or four weeks. A few, because of a rapid growth of natal hair or because of its special distribution that causes it to grow into the wound, will require more time, closer watching

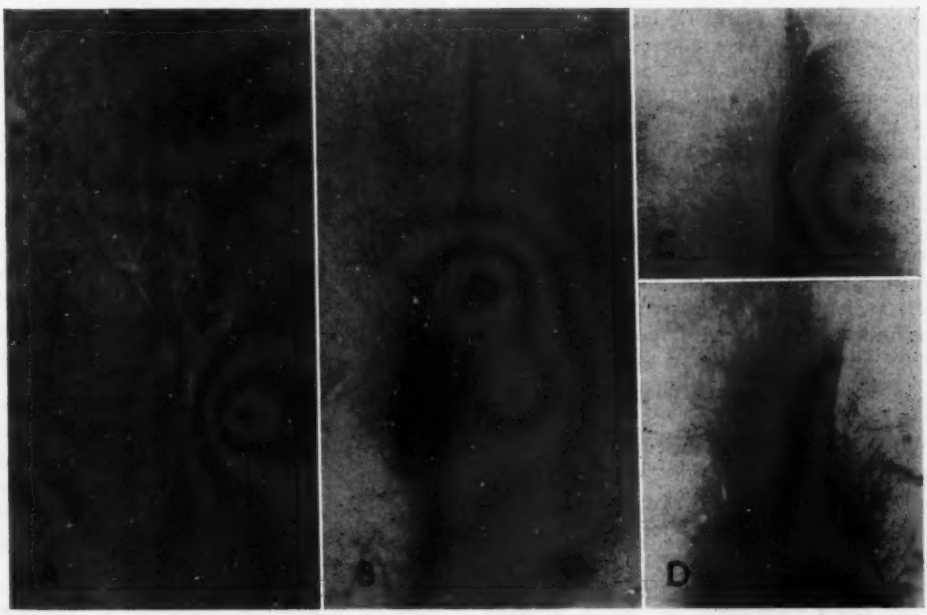

Fig. 9 (A, B, C and D)
Typical scars of healed cases.

and meticulous care. Operations performed in the summer tend to heal slowly because of excessive perspiration and maceration of the wound. Greater restriction of physical effort during this season is necessary. Transferring postoperatives to the reconditioning section and allowing physical freedom with slight limitations interferes little with healing. Maintaining bodily vigor and morale warrants the continuance of this practice. As the cavity disappears the incised skin is gradually drawn together by a narrow scar that is painless and movable. Regardless of the number of side tracts, epithelization is from the periphera toward the center. Demonstrable pitting in the natal fold should be included in the incision of the major cavity to prevent the possible formation of secondary cysts at a later date.

Six hundred and eighteen cases have been treated in the above described manner. Though in time of war a follow-up on military cases that have surgery is difficult, there was some opportunity for observation. None was released until symptom free. Others returning from combat for re-assignment were observed. Some military personnel assigned to fixed installations have been available for periodic follow-up over a period of three years. Of the cases available for follow-up, eight have required additional care. Five had a breakdown of their scars because of trauma or ingrowing hair. Three had remaining cyst formation at the end of the scars, indicating that the initial incision had not been of sufficient length to expose the entire cavity. These healed promptly after incision under local anesthesia and treatment with Carnoy's solution. Twenty-four cases treated by this method in civilian practice are included in this series. Some are at present six years old and all have remained well.

SUMMARY

(1) The pathology of pilonidal cysts and sinuses is briefly described.

(2) A method of treatment by eventration of the sinus cavity is detailed.

(3) Gratifying results have been obtained in 618 cases treated by this method.

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"PENTOTHAL" FOR TONSILLECTOMY IN CHILDREN*

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"Pentothal"[1] is a routine drug at this hospital for tonsillectomy in adults and over 500 cases have already been performed without serious complication. As early as 1942 "pentothal" was used by one of us (S. L. F.) in adult tonsillectomies.[1] Subsequently a report by Griffiths and James appeared in 1945 in which "pentothal" was used in adult tonsillectomies.[2] The technic which we developed proved so successful in adults that we decided to apply the same procedure in children. Accordingly thirty-five children were anesthetized with "pentothal," the youngest in the series being two years of age, the oldest ten (*Table 1*).

Technic.—There are several important factors in administering "pentothal" for tonsillectomy in either adults or children. It is necessary to maintain a clear airway with adequate exposure of the field of operation. For this purpose we have found the Davis mouth gag ideal since it permits the simultaneous administration of nitrous oxide and oxygen (*Fig. 1*). The second important factor is the use of nitrous oxide (or ethylene) under pressure as an analgesic in order to diminish the total dose of "pentothal."

The Davis gag is obtainable in both child and adult sizes, in shapes to accommodate the left-handed or right-handed surgeon and the edentulous as well as the mouth with a full complement of teeth. It is essential to use the correct size in order to maintain a clear airway. In *Fig. 2* the relationship of the opening in the blade of the gag with the epiglottis can be visualized. When 70 per cent nitrous oxide and 30 per cent oxygen are forced through the opening under pressure, the patient breathes the gas mixture because room air is actually forced out of the mouth by the excess, high pressure nitrous oxide-

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ANALYSIS OF CASES IN WHICH "PENTOTHAL" WAS USED IN CHILDREN

Hospital Number	Age	Length of Operation (minutes)	Amount of 2½ per cent solution "Pentothal" Used (c. c.)	Reaction Time (minutes)
32956	8	30	17	immediate
31882	4	25	20	immediate
32906	2	30	10	10
32098	8	30	17	5
32821	3	30	17	5
33069	4	25	24	5
33070	5	40	17	10
E. M.	2	25	10	15
33002	5	30	9	4
33235	4	35	13	immediate
33234	6	35	14	15
33233	4	30	15	10
33278	7	30	14	3
33401	5	30	11	4
33296	8	30	16	5
33331	9	30	20	immediate
33427	5	60	20	10
25612	10	20	20	20
33436	6	40	15	10
33435	8	40	13	10
33452	10	45	20	10
33472	8	35	20	15
33286	9	40	40	10

Table 1

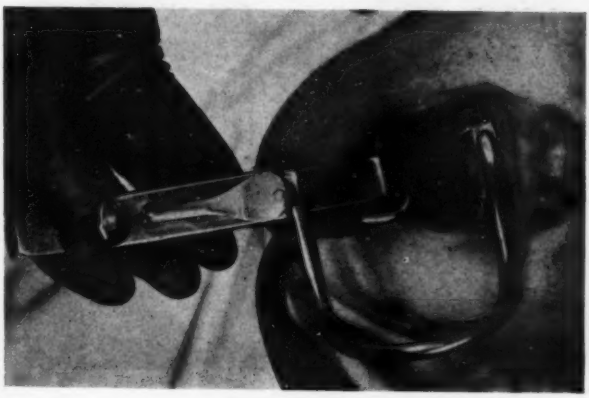

Fig. 1
The Davis gag in place.

oxygen mixture. In this way nitrous oxide analgesia is administered with certainty, and the over all dose of "pentothal" is reduced by as much as 50 per cent.

After venipuncture a test dose of 1 or 2 c. c. of 2½ per cent solution of "pentothal" is administered to determine the patient's tolerance to the drug. When this has been determined "pentothal" is injected slowly and cautiously in the child, whereas in the adult it is injected in larger amounts of from 5 to 10 c. c. at one time. The Davis gag is then gently inserted with the nitrous oxide and oxygen blowing through the blade of the gag. An assistant, not the anesthetist, should support the gag. This permits the anesthetist to devote his undivided attention to the color of the finger nails, the anesthetic machine, respiration, and so on. An anesthetic machine capable of delivering gases under pressure should be used (*Fig. 3*).

After the initial injection of "pentothal" and insertion of the gag, the tonsillectomy is begun. Additional "pentothal" is not injected until the surgeon informs the anesthetist that the swallowing reflexes have returned. In children, small amounts of "pentothal" are injected with extreme caution; in adults larger amounts are injected with relative safety. In general, the first sign which indicates that the patient needs more "pentothal" is the return of the pharyngeal reflexes. If respiration becomes irregular or the finger nails begin to lose their pink color it is in most cases due to the assistant's relaxing the gag, which results in an obstructed airway. This, of course, is easily remedied by "pulling up" on the handle of the gag.

Should a laryngospasm occur the nitrous oxide is turned off, 100 per cent oxygen is forced through the gag, and no additional "pentothal" is injected since "pentothal" tends to potentiate the spasm rather than relieve it. As carbon dioxide is built up because of the spasm it is important to maintain the integrity of the respiratory center and not paralyze its ability to innervate the muscles of respiration and the vocal cords

by deepening the patient with further "pentothal." Should the spasm persist, atropine may be injected into the "pentothal" tubing. Curare may also be injected to relieve the spasm but it is important to use a separate vein, as a precipitate forms when the two drugs mix.

Premedication in children consists of atropine only. The dose was never smaller than 1/250 grain hypodermically one hour preoperatively. In the adult "pantopon" was used with atropine, the average adult dose being "pantopon" grain 1/3 and atropine grain 1/100. It was our experience that "pantopon" predisposed less to laryngospasm than did morphine.

Fig. 2
The relationship of the tongue blade in the Davis gag to the epiglottis and larynx.

The average amount of 2½ per cent solution of "pentothal" required for an adenotonsillectomy lasting 30 minutes in an adult is 30 c. c. The average amount in a child under 10 years is 15 c. c. In children 1.0 to 1.5 c. c. of metrazol is injected intravenously immediately after the operation. Metrazol has not been found necessary in the adults since they react much more quickly.

OBSERVATIONS

Although "pentothal" for tonsillectomy proved successful in children, we feel that its routine use is not practical in children under ten years of age. It is the anesthetic of choice in individuals over age ten in whom veins are readily

Fig. 3
The administration of "pentothal" during tonsillectomy, showing the assistant supporting the Davis gag, and nitrous oxide and oxygen being administered simultaneously.

located. There are several reasons for discouraging the use of "pentothal" for tonsillectomy in children under age ten. The veins of children are small and venipuncture often becomes a time-consuming and difficult procedure. Dislodgment of the needle is frequent because it is necessary to exert more caution and inject smaller doses of "pentothal." This lighter plane of anesthesia may result in dislodgment of the needle due to jerking of the arm. To find other accessible veins in a child is obviously difficult, and a switch to ether at this point is often dangerous because of laryngospasm and possible aspiration of blood and secretions from the throat. In addition, children under ten frequently remain sleepy for hours following operation even though their reaction time is usually less than ten minutes. They will answer questions and respond to stimulation very quickly without the nausea and vomiting seen in the postoperative ether patient. However, they desire sleep and are not so active postoperatively as those children who had ether instead of "pentothal." During this longer and more persistent sleeping period, unsuspected bleeding from the throat or nasopharynx may escape detection.

CONCLUSIONS

"Pentothal" for tonsillectomy in children is feasible. For the reasons enumerated, however, it is not advocated for children undergoing tonsillectomy who are below the age of ten.

It is recommended that the Davis mouth gag be employed and that the "pentothal" be supplemented with nitrous oxide and oxygen.

It is felt that "pentothal"-nitrous oxide for tonsillectomy in adults and older children is the anesthetic of choice.

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REIMPLANTATION OF THE URETER INTO THE KIDNEY PELVIS FOLLOWING AVULSION*

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Uretero-pyeloneostomy is the term applied to the reimplantation of the ureter into the kidney pelvis. This procedure was first attempted by Trendelenburg in 1886 for a stricture at the uretero-pelvic juncture. This was unsuccessful. It was again attempted by Küster in 1891, this time successfully. These early attempts, though, were for a plastic correction of a hydronephrosis. Bazy introduced the term uretero-pyeloneostomy to urology at the Thirteenth International Congress at Paris in 1900. Since that time, various procedures have been introduced by Fenger, Schwyzer, Walters, Foley, etc., for the correction of uretero-pelvic obstructions.

The procedure of uretero-pyeloneostomy has been varied and has been improved by Küster, Quinby, Von Lichtenberg, Walters and Braasch, Lubash, and Hyman and Wilhelm. Eleven cases of uretero-pyeloneostomies were reported by Hyman and Wilhelm in 1941, four of which were unsuccessful.

Accidental avulsion or severance of the upper ureter from the renal pelvis during operations on the kidney has been reported ten times. A case was reported by Begg in 1926 and a case by Cowden in 1928. Bailey, in 1928, reported avulsion of the ureter and pelvis from the kidney with successful resuturing. Harris reported another case in 1930. The most extensive series of accidental avulsion of the ureter from the pelvis was reported by Hyman and Wilhelm in 1941. They collected five cases from the records of Beth Israel and Mt. Sinai hos-

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pitals in New York City over a ten-year period.

In December, 1935, the senior author of this paper reported a case in his paper, "Accidents in Renal Surgery," before the New York Academy of Medicine. The case in question was case 21, a woman, aged twenty-six, who was operated upon for a right hydronephrosis. Accidental avulsion of the ureter complicated a pyeloplasty. The outcome of the reimplantation of the ureter into the most dependent part of the pelvis was entirely successful.

The case we present below is the eleventh such case to reach the literature. In addition, this case has an unique feature, not reported heretofore, in that a patent, adequate stoma at the uretero-pelvic junction is present together with normal ureteral peristalsis and pelvic muscular action persisting after severance of the continuity of the pelvis and ureter. This muscular action was demonstrated by the subsequent passage of two calculi from the kidney in question. This event supports the experimental work of Wharton, wherein he proved the independence of the ureteral innervation from the renal pelvis above and the bladder below. He showed that the abdominal nerve plexuses are responsible for the innervation of the whole ureter.

CASE REPORT

Y. B. (*8334*), age 62, was first seen in August, 1944. She had a history of having a "kidney condition" for the past eight years, and that she had passed pus in her urine rather frequently. About five weeks prior to coming to the office, she had an attack of acute gastritis and vomited a great deal. Since that time, she had passed a great deal of pus in her urine and had also noticed on several occasions that her urine was reddish in color. Chills and fever were present at first, but not at the time of examination. There was no associated frequency or burning on micturition.

Systemic examination revealed arteriosclerotic heart disease with an enlarged heart, and healed varicose ulcers on the right leg.

Urological examination revealed tenderness on abdominal examination; the tenderness was elicited in both sides of the abdomen and in the lumbar regions. Examination of the external genitalia revealed no urethral or vaginal discharge. A catheterized specimen of urine was cloudy with a specific gravity of 1.016, albumin 1 plus, sugar negative, and, microscopically, many pus cells were present.

A plain x-ray of the abdomen revealed a shadow about the size of a lima bean in the region of each kidney. The right kidney shadow was lower than the left. An intravenous pyelogram revealed the solution as appearing in normal time on both sides. Both pelves and calices were dilated. On the left, the shadow appeared to be in the pelvis of the kidney. On the right, the shadow appeared to be in the lower calyx and the

Fig. 1
Preoperative intravenous pyelogram demonstrates a dilated pelvis in a ptotic idneyk with uretero-pelvic obstruction.

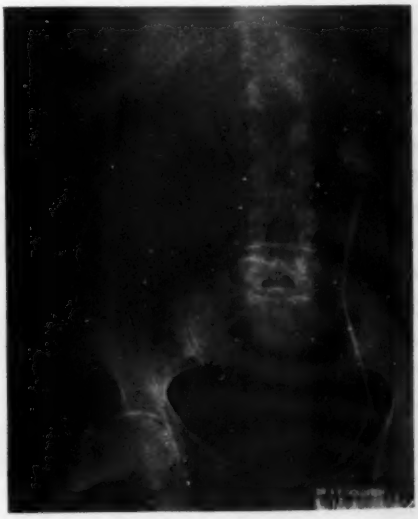

Fig. 2
Postoperative retrograde pyelogram demonstrates patency of the repaired uretero-pelvic junction iwth good drainage and no angulation.

ureter was dilated. In the upright position, the right kidney dropped lower than normal. Under sodium pentothal anesthesia, cystoscopy was performed. The trigone was of normal color. There was an absence of any intravesical bulging, edema, stone, diverticulum, ulceration or tumor in the bladder. A number 5 ureteral catheter was passed up each ureter without encountering any obstruction. A few pus cells were found in the urine from each kidney, more on the right than on the left. Intravenous phthalein appeared in six minutes from the left kidney with a 22 per cent concentration in the first fifteen minutes. The urine from the right kidney, collected transvesically, showed a concentration of twelve per cent in the first fifteen minutes.

The patient was admitted to Sinai Hospital on August 29, 1944, with a temperature of 100° for an operation upon the left kidney. The admission urine had a specific gravity of 1.022 with a trace of albumin, negative sugar and microscopically loaded with pus cells and three red cells per high power field. The blood count revealed 76 per cent hemoglobin, 3,550,000 red blood cells, 6,300 white blood cells with a differential of 34 per cent small lymphocytes, 2 per cent large mononuclear cells, 2 per cent transitional cells and 61 per cent neutrophils and 1 per cent eosinophils. The blood urea on admission was 33 milligrams per cent. On August 31, 1944, the left kidney was delivered through the usual Israel incision. The ureter was picked up and a tape placed around it. The peripelvic fat was removed and it was observed that the pelvis was dilated. No aberrant vessels were found but the renal artery was posterior to the ureter. The pelvis was then opened posteriorly and a triangular stone measuring twelve millimeters in diameter was removed. The ureter was of normal caliber, but formed a marked angle with the pelvis. On dissecting the uretero-pelvic juncture, the ureter was accidentally pulled away from the pelvis. In view of the fact that the opposite kidney had a calculus, we decided to repair this defect. A second opening was made in the pelvis for the reimplantation of the ureter. The reimplantation was done by taking three plain catgut sutures and one No. 1 chromic gut suture through the serosa of the ureter, which was then brought into the new opening of the pelvis. A ureteral catheter was placed from the opening made for the removal of the stone, through the pelvis down through the ureter. The incision in the pelvis was not sutured. Two cigarette drains were placed down to the opening in the pelvis. The kidney was replaced in its cavity. Closure was made in the usual manner. The postoperative course was normal and the temperature returned to normal on the third postoperative day. Urine drained from the pyelostomy wound as well as through the catheter. The latter was removed on the thirteenth postoperative day. On the sixteenth postoperative day, the wound was dry and the patient was discharged from the hospital.

Three months later, she was again cystoscoped under sodium pentothal anesthesia. The urine from the left kidney showed no pus cells. The urine from the right showed many pus cells. A left retrograde pyelogram revealed a definite hydronephrosis with some interruption of visualization in the left ureter. No obstruction was encountered in passing a catheter into the left kidney.

On February 5, 1945, she was readmitted to the hospital and the calculus was removed from the right kidney. Her hospital stay was interrupted by a complication, a right bronchopneumonia and pleural effusion. This was soon controlled with sulfonamides and penicillin. She was discharged on February 23, 1945, and shortly thereafter the wound healed completely. There were some pus cells in the urine, but this soon cleared after sulfa therapy.

On July 30, 1946, (two years after her operation upon the left kidney) she came to the office complaining of pain on the left side, following which she passed a stone the size of a pea. A plain roentgenogram at that time revealed no further radiable shadows suggestive of calculi. An intravenous pyelogram was also taken and revealed the solution to appear in normal time in both kidneys. Subsequent films revealed a slightly dilated pelvis on the left with a slightly dilated ureter. The uretero-pelvic juncture seemed satisfactory, excepting a portion which was slightly dilated. The "diodrast" was somewhat delayed in leaving the pelvis on the left. Microscopic examination of a voided specimen showed 25 to 35 red blood cells to a high power field. One week later, she again experienced an attack of pain on the left side, and she again passed a stone about the size of a pea. Roentgenogram taken at this time failed to reveal shadows suggestive of any other urinary calculi.

DISCUSSION

Etiology and Indications.—Uretero-pyeloneostomy, according to the literature, is a procedure only rarely attempted. Electively, it has been attempted by Trendelenburg, Küster, Quinby, Von Lichtenberg, Walters and Braasch, Hyman and Leiter, Hyman and Wilhelm, Lubash, Wilhelm and others, the majority of which were successful. In 1927, Quinby reported seven cases which he successfully reimplanted for hydronephrosis. Hyman and Wilhelm in 1941 reported their attempts at this procedure in eleven cases.

All the cases of avulsion of the ureter from the renal pelvis, occurred during a pyelotomy for a calculus with the presence of infection, except the case cited by Goldstein in his "Accidents in Renal Surgery." In the reported cases, the pelvis was thinned and ulcerated by the infection, and irritated by the calculus. Traction of the ureter then resulted in its being torn from the pelvis. A contributing causative factor, in addition to excessive pulling, was the presence

of a friable, markedly inflamed pelvic mucosa. In each of the eleven cases reported, an attempt was made to save a functioning kidney by the reimplantation of the avulsed ureter into the kidney pelvis.

Complications.—The complications that may follow an operative procedure of this kind are:

(1) Separation of the ureter from its new insertion.

(2) Perinephric infections.

(3) Strictures at the uretero-pelvic juncture. This may be an early or late stricture.

(4) Obstructions due to a mucosal fold.

(5) Secondary hydronephrosis.

(6) Secondary hydronephrosis with infection, pyelonephritis or cortical abscesses.

(7) Formation of calculi.

(8) Persistent urinary fistula.

The presence of infection together with intrapelvic tension on the suture lines may result in separation of the ureter from the pelvis with extravasation of the infected urine into the perirenal areas. The resulting perirenal abscess necessitates incision and drainage. Frequently, one encounters early stricture at the anastomotic site. This occurred in Hyman and Wilhelm's series, in two of their five cases of avulsion, and in four of their six cases of reimplantation for uretero-pelvic obstruction. Another not uncommon postoperative complication is late stricture, and this occurred in one of five cases of avulsion and one of the six of reimplantation, of the eleven cases reported by Hyman and Wilhelm. A persistent urinary fistula may remain and drain through the lumbar incision particularly following the persistence of a postoperative ureteropelvic stricture.

Should a postoperative stricture result, whether due to scar formation or to a mucosal valve or diaphragm, it will necessitate prompt and repeated cystoscopic dilatations; otherwise, progressive narrowing of the stoma will occur with secondary hydronephrosis. This latter complication, especially in association with an infected kidney, soon leads to a non-functioning unit, defeating the original intent of the operative procedure.

A very novel procedure was adopted by Hyman and Leiter in relieving an obstruction at the new anastomotic site caused by a mucosal valve. A cystoscope was introduced through the pyelostomy wound, the pelvic mucosal flap was visualized and removed by electrocoagulation. The obstruction was adequately removed and the results were entirely satisfactory.

Another complication that can occur in many with a calculus-forming diathesis, is the subsequent formation of calculi requiring secondary operative procedures. Calculi, too, may result following through and through suturing of the ureter to the pelvis, the calculi forming on the intrapelvic portion of the suture material.

Due to the formation of excessive adhesions following the initial operation upon the kidney, a secondary operative procedure on the same kidney is usually very difficult. The complications enumerated above or any pathological conditions that may subsequently develop in the kidney in question frequently necessitate a secondary nephrectomy.

TREATMENT

In order to prevent most of the complications discussed, the accepted surgical procedures of free urinary drainage by an adequate pyelostomy or nephrostomy together with splinting of the ureter and adjacent pelvis by a ureteral catheter must be utilized. As advocated by Walters, and Hyman and Wilhelm, accurate apposition of the ureter and pelvis in suturing the anastomosis is also very helpful.

The nephrostomy tube, by draining away the urine as fast as it is formed, prevents undue tension on the suture lines, and also establishes adequate drainage for an infected renal pelvis. In our case, a nephrostomy tube was not employed. A pyelotomy was performed for the introduction of a catheter to protect the anastomosis. Adequate drainage was obtained through the pyelotomy incision by bringing two cigarette drains to it. Hyman and Wilhelm have pointed out that local antibiotics can be used through a nephrostomy tube to counteract the renal infection. They maintain the nephrostomy tube in situ for at least two weeks, and before its removal it is clamped off for a few days in order to put the new stoma to a practical functional test.

The splinting ureteral catheter insures the patency of the newly formed stoma and also immobilizes the anastomosis and so facilitates quicker repair. Hyman and Wilhelm advocate leaving this splinting catheter in situ for at least ten days as its early removal may result in stricture or in complete occlusion as occurred in one of their cases. In our case, the ureteral catheter was removed on the thirteenth postoperative day.

Thirdly, accurate approximation of the sutured parts should be closely watched. One should try to prevent the formation of a mucosal valve or diaphragm and also to prevent any undue tension at the anastomosis, or failure of the anastomosis will result. Here, too, one should not perforate the lumen of the pelvis, as the presence here of the suture material in contact with the urine acts as a nidus for further calculus formation.

Finally, for maintenance of good renal function, periodic pyelographic studies and cystoscopic dilatations should be performed.

CONCLUSIONS AND SUMMARY

The rarity of these cases makes their reporting essential in order to be able to determine the best approach to conservative urological surgery compatible with the preservation of the maximum amount of functional renal tissue. It is particularly applicable to plastic approaches for the relief of uretero-pelvic obstructions and hydronephrosis.

In this paper, the literature is reviewed and uretero-pyeloneostomy is discussed. Eleven cases of avulsion of the ureter from the renal pelvis have been reported including those of the authors, the authors' case being the first to have proven the adequacy both physically and physiologically of the newly formed stoma by the subsequent development and expulsion of two stones from the affected kidney. It is also pointed out that in the performance of a ureteropyeloneostomy, one should rely upon an adequate pyelostomy or nephrostomy, splinting of the ureter, and accurate suturing at the anastomosis. It is essential that a provision for urinary drainage be made by the employment of a pyelostomy, or by the employment of a nephrostomy tube, when the latter procedure is thought advisable.

We did not employ a nephrostomy tube in our case because the presence of the nephrostomy tube initially would prevent the utilization of adequate pressure sutures in the kidney for the control of primary hemorrhage from the nephrostomy site; and secondarily, because of the ever present possibility of a complicating secondary hemorrhage when pulling out the nephrostomy tube. Other factors should also be considered that mitigate against the use of a nephrostomy tube, such as the production of an area of pressure necrosis in the kidney abutting the nephrostomy tube. Furthermore, infection (intrarenal and perirenal) and concomitant pyelonephritis easily manifest themselves at the site of a foreign body (nephrostomy tube) and local necrosis.

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EXPERIENCES WITH SODIUM "PENTOTHAL"*

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Many drugs such as morphine, alcohol, "avertin," procain, ether, and numerous barbiturates have been injected intravenously to produce anesthesia. My first contact with intravenous anesthesia was in 1929 when as an intern I watched E. H. Lancaster of Houston inject 1 gram 10 per cent of sodium "amytal" intra-

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venously as a basal anesthetic in gynecologic cases. The patients slept all day and were generally too depressed for their own safety. In 1935 I started using "evipal" for minor operations of short duration such as dilatation and curettage and incision and drainage. Ten per cent solution was used and proved adequate for the surgery. About 50 per cent of these cases showed post-anesthetic delirium and in two cases this lasted for several hours in a rather violent extent.

About 1937 I changed from "evipal" to sodium "pentothal" and found it much more satisfactory as respiration was better and post-anesthetic delirium was lacking. I used 5 per cent solution injected intermittently for minor cases of short duration and for induction in the nervous patient. During the war two portable surgical hospitals assigned with me to the Chinese VIII Army used intermittent 5 per cent sodium "pentothal" in all traumatic surgery except abdominal cases. It was used with no supplementary anesthesia as syringe, tourniquet airway, and Yankhauer mask was all the equipment available. The patients were all Chinese in poor condition and the anesthetic-surgical mortality rate was rather high.

Last year I returned to this country and all the conveniences of a modern operating room and began the use of 2½ per cent sodium "pentothal" with 50-50 nitrous oxide-oxygen.[1] We used it in cases requiring relatively light anesthesia and gradually lengthened the time until we were using it in some 3-hour cases such as spinal fusions.[2] We found that we used less "pentothal" if we diluted it after the first 20 c. c. One gram was diluted to 40 c. c., 20 c. c. removed for use, and the remaining 20 c. c. diluted to 40 c. c. with distilled water giving a 1¼ per cent solution. Twenty c. c. of the 1¼ per cent solution was used and the remainder diluted to ¾ per cent with 20 c. c. of distilled water and this strength was used after the first two hours.[3] Pentothal was given intermittently from a 20 c. c. or 50 c. c. syringe (with a syringe holder or not) with a short length of rubber tubing attached directly to the needle in short cases and attached to the saline drip in long cases.

One can see that we were working toward the use of more dilute solutions and I now almost routinely use 0.4 per cent solution in a continuous drip except for inductions or very short cases.[4] With 0.4 per cent made up 2 grams of "pentothal" in a 500 c. c. Baxter flask of saline or 5 per cent glucose in saline, the administration is simplified and I feel that I use about 30 per cent less "pentothal" in cases lasting over an hour than I did with the intermittent 2½ per cent solution. Simply do the venipuncture with a 19-gauge needle connected to the ordinary intravenous saline set up and regulate the flow by the drip bulb. The advantages of the drip method are: the ease of use, the needle does not stop up, "pentothal" can be started early and dripped slowly if the surgeon is not ready, and there is less early depression. The advantages outweigh the disadvantages which are: a large needle must be used, and it is difficult to give large quantities of blood or saline with it. The latter does not worry me as I rarely use "pentothal" in cases in poor condition. My usual procedure is to drip or run the 0.4 per cent solution rather rapidly until the patient is asleep, then cut down the flow and start 80-20 nitrous oxide-oxygen. If for some reason, the "pentothal" will not run rapidly, or the patient will not relax, it is easy to put the canister in and add cyclopropane to the nitrous oxide-oxygen mixture already in the bag. Ordinarily, I run one liter of oxygen and four liters of nitrous oxide for about 10 minutes, then dump the bag, refill; and then run only basal oxygen which amounts to from 200 to 600 c. c. per minute. About every 30 minutes I dump the bag and refill with an 80-20 mixture. Occasionally it is necessary to run as high as 35 per cent oxygen to keep the patient in good color. For those who use this method on patients in poor condition, I recommend a 50-50 mixture of nitrous oxide-oxygen.

It is my opinion that the arterial oxygen is maintained at or above normal when nitrous oxide-oxygen is used in conjunction with "pentothal" and that the amount of "pentothal" used is cut in half in cases lasting over 30 minutes. Halving the amount of "pentothal" used in long cases decreases respiratory depression and makes for a more rapid awakening of the patient. Moderate amounts of morphine and scopolamine

given 1 hour before anesthesia also decrease the amount of "pentothal" used with safety to the patient as well as postoperative relief from pain. I routinely use morphine before "pentothal" but no other barbiturates as they are much more depressing to the respiration than "pentothal." I have never used over 2 grams of "pentothal" in any one patient and in the last 100 consecutive cases which I would like to report the maximum dose has been 1.7 grams.

One hundred cases are reported with a total of 79 hours 50 minutes of anesthesia. Each case averaged 48 minutes duration and used 0.58 gram of "pentothal" for an average of 0.012 gram a minute. No supplement was used in two blood pressure studies. Nitrous oxide with 20 to 35 per cent oxygen was used to supplement the remaining 98 cases, with cyclopropane being added in 8 cases as follows: 2 hernias, 1 appendix, 1 vaginal hysterectomy, 1 breast, 1 tonsil, 1 esophagoscopy, and 1 fracture. The amount of "pentothal" needed varied widely in various patients.[5] The last case mentioned was a 300-lb. man with an old fracture of the elbow who absorbed the "pentothal" drip at the average rate and did not even go to sleep so that cyclopropane was added throughout the 2¼ hours of the operation. This patient also required 600 c. c. of basal oxygen to maintain a full bag.

One of the favorite uses of "pentothal" was for dilatation and curettage which averaged 17 minutes and required 0.4 gram or 0.023 gram per minute. This large dose over a short period left 2 of the 22 cases depressed and metrazol[6] and oxygen were given at the end as the patients stopped breathing when the surgery stopped. One case was a momentary depression but the other lasted for 10 minutes. Two other cases were given metrazol as they appeared depressed when put in bed and a fifth case was given metrazol as she was an outpatient and I feel that metrazol gives a definite shortening of the waking time. The other 95 cases received no metrazol and practically all of them were awake enough when put to bed to answer questions.

The most suitable cases in my series for "pentothal" were orthopedic cases and skin grafts which lasted over one hour. The orthopedic cases required 0.009 gram per minute and the plastic cases only 0.007 gram per minute. Next most suitable for "pentothal" were small hernias, vein ligations and breast operations. In all of these cases the surgeon was out of the way, leaving me complete control of the airway. When I use "pentothal," I want control of the airway and rarely use "pentothal" for surgery about the face. Sometimes I get talked into things and you will note that there are 2 tonsillectomies and one esophagoscopy in the series. One of the tonsil cases was intubated and the other received nitrous oxide-oxygen by nasal airway. Neither tonsil gave me any trouble but the esophagoscopy was a mess. The surgeon had previously tried unsuccessfully to esophagoscope this woman under local. I gave her 1½ grams of "pentothal" rapidly and could not even open her mouth; then I gave her 3 c. c. of curare, intravenously[7] and still could not open her mouth or do a blind nasal intubation; so I quickly turned on a heavy flow of cyclopropane for about 10 minutes and then did a nasal intubation under direct vision. Since this I have used open drop ether in similar cases with no trouble. I feel that any cases intubated under "pentothal" should have the throat and cords cocainized[8] previous to the "pentothal" and even then I have trouble with laryngospasm and coughing.

In looking over the recent literature I note that others agree with me wholly or in part. Damarjian[9] reported 200 cases done in the C.B.I. Theatre on Chinese soldiers with the following results: 0.035 gram per minute was used where no morphine or nitrous oxide was given; 0.020 gram per minute was used when morphine was given but no nitrous oxide used, and only 0.011 per minute was used when morphine premedication plus a 50-50 nitrous oxide-oxygen mixture was used.

Barton, Wicks and Livingston[10] took four blood samples in dogs and in humans: (1) before anesthesia; (2) after "pentothal;" (3) after "pentothal" and oxygen; (4) after "pentothal" and nitrous oxide-oxygen (50-50). They found that the arterial oxygen remained the same in specimens 1 and 2 in humans; but the arterial oxygen was increased during anesthesia (3) with "pentothal" and oxygen and (4) with "pentothal" and nitrous oxide-oxygen. The increased arterial oxygen was about the same in (3) and

(4) but it took 4 times as much "pentothal" to produce anesthesia with "pentothal" and oxygen as it did to maintain anesthesia with "pentothal" and nitrous oxide-oxygen. "Pentothal" alone required 0.020 gram per minute to maintain anesthesia, "pentothal" and oxygen required 0.021 gram per minute, while "pentothal" and nitrous oxide-oxygen required only 0.005 gram per minute. This shows that the combined use of "pentothal" and nitrous oxide-oxygen markedly reduces the amount of "pentothal" necessary for anesthesia while maintaining the arterial oxygen above normal.

SUMMARY

A brief resume of the author's experiences with sodium "pentothal" is given and the last 100 consecutive cases are reported.

QUANTITY OF "PENTOTHAL" USED

Operation	No. Cases	Total Time Hr. Min.	Total Amt. Grams	Avg. Time Hr. Min.	Avg. Amt. Grams	Amt. Per Min. Grams
Dilators and curettage	22	6:15	9.0	:17	0.4	0.023
Orthopedic, arm and leg	22	25:00	14.0	1:8	0.63	0.009
Miscellaneous minor	12	5:30	7.7	:27	0.64	0.023
Skin graft	8	9:45	4.5	1:13	0.56	0.007
G. U., cysto-resection, etc.	7	5:00	4.3	:43	0.61	0.014
Induction for Lap.	5	5:20	1.5		0.3	
Hernia	5	6:45	4.1	1:21	0.8	0.010
Vein ligation	4	5:00	3.2	1:15	0.8	0.010
Breast operation	3	2:00	1.3	:40	0.43	0.010
Tonsillectomy	2	1:30	1.1	:45	0.55	0.012
Supplement, spinal and block	2	1:00	.8	:30	0.4	0.013
Vaginal	2	3:15	2.4	1:37	1.2	0.012
Blood pressure studies	2	:20	0.5	:15	0.5	0.050
Jaw case	1	:15	0.05	:15	0.5	0.033
Pelvic examination	1	:10	0.5	:10	0.5	0.050
Brain trephine	1	1:15	0.8	1:15	0.8	0.010
Encephalogram	1	:45	0.6	:45	0.6	0.013
Esophagoscopy	1	:45	1.5	:45	1.5	0.033
Total	100	79:50	58.8	:48	0.588	0.012

No supplement was used with the two blood pressure studies.

Nitrous oxide with 20 to 35 per cent oxygen was used to supplement the remaining 98 cases, with cyclopropane added in 8 cases as follows: 2 hernias, 1 appendix, 1 vag. hysterectomy, 1 breast, 1 tonsil, 1 esophagoscopy, and 1 fracture.

The following are listed as contraindications[11] to the use of sodium "pentothal;" depressed respirations, shock, overdose of morphine or barbiturates, bronchiectasis, severe anemia, coronary cases, liver damage, neck infections or tumors, poor veins, rectal surgery or any surgery requiring deep anesthesia at the end of operation.

CONCLUSIONS

(1) "Pentothal" is indicated for surgery requiring light anesthesia of any duration.

(2) It is best for the anesthetist to have some access to the patient's airway.

(3) The most suitable way to give "pentothal" for anesthesia lasting over 20 minutes is in dilute solution by a continuous drip.

(4) "Pentothal" is safest used when combined with nitrous oxide or nitrous oxide and cyclopropane. Nitrous oxide and "pentothal" are useful separately, but dangerous if either is pushed. If combined, the disadvantages are eliminated and usefulness increased.

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DISCUSSION (*Abstract*)

Dr. John Adriani, New Orleans, La.—Have you any deaths in your personal cases in this country?

Dr. Brady.—No, sir.

Dr. Hiram R. Elliott, Fairfield, Ala.—In discussing sodium "pentothal" for tonsillectomies, most of us will agree that it is not the anesthetic of choice for these operations. But if, for various reasons, we feel that we want to use it, then, if we spray the throat and nasal passages two or three times with either 10 per cent cocaine solution or 2 per cent "pontocaine" solution, we

can get along very well if the patient is put in the Trendelenburg position and the free blood sucked from the throat. This free blood irritates the vocal cords, is quite likely to cause the patient to cough, and may lead to a laryngospasm.

Frequently we like "pentothal" sodium for induction when we are going to use some form of inhalation anesthetic. On some occasions we have sprayed the throats of these patients. As a result we have found that the switch-over to the inhalation anesthetic was smoother.

Dr. Julius D. Holly, Miami Beach, Fla.—I have given about 150 "pentothal" anesthetics for tonsil work, and I feel that the most important thing in this type of anesthesia, is to get the patient in the third stage of anesthesia before starting the surgical procedure. An airway is then inserted, nitrous oxide 2 liters and oxygen 300 c. c. are then administered through the airway by means of a hooked catheter, for about one minute. The nitrous oxide is discontinued, and oxygen is administered through the hooked catheter which is attached to the angle of the lips. The patient is then given "pentothal" at frequent intervals to maintain anesthesia. Another important point to remember in giving "pentothal" for tonsil work, is to place the patient in the extreme Trendelenburg position, so that secretions will not accumulate in the region of the larynx. Premedication employed consists of "seconal" grains 1½ or "nembutal" grains 1½ and atropine sulphate grains 1/150 given 30 minutes before the posted time of operation.

I have administered about 10,000 "pentothal" anesthetics and feel that neither age nor pathological conditions of the patient are contraindications for its use. In fact, I am of the opinion that the sicker the patient, the more the indication for the use of "pentothal." I have given "pentothal" sodium to a 10-day-old infant, who had a ruptured appendix, and to a man 101 years old who had a prostatic operation. My experience with "pentothal" has been so gratifying, that I have adopted a motto, "If I can get into a vein, I will give 'pentothal.'"

I can see no logical reason for the continuous-drip method of "pentothal" administration, as I feel, by this method unnecessary amounts are administered. We are well aware of the fact, that after anesthesia has once become established, only small amounts (1-2 c. c.) are required, from time to time, to maintain surgical anesthesia.

I employ a self-constructed syringe holder (a pipette stand) which holds 2 20-c.c. syringes. A three-way stop-cock is used, so that "pentothal" can be given intermittently with glucose. The glucose supplies parenteral fluids and at the same time prevents clogging of the intravenous needle. When "pentothal" is given by the intermittent method, you give only the amount needed to maintain a certain depth of anesthesia. I do not depend upon percentages because patients differ as to tolerance to "pentothal" sodium.

I never employ morphine with "pentothal," because I feel that it is unwise to give two respiratory depressants.

Dr. Geo. C. Austin, Miami, Fla.—I was extremely impressed with the use of "pentothal" by continuous drip. I have been using continuous drip mostly in conjunction with spinal anesthesia, and I find I can keep the patient happy during surgery and have him awake at the conclusion and use an amazingly small quantity of "pentothal." I have had several with continous drip, a half gram in 1,000 c. c. solution, using half that quantity for a three-hour procedure. The patient was asleep throughout the entire procedure and was awake when returned to his room. It seems like an infinitesimal amount of "pentothal," but it does the work. "Pentothal" is one of our best anesthetics, if used properly. I feel it should not be used in children. I like morphine preceding "pentothal," providing I can order the dose given. I do not like the surgeon to prescribe a quarter grain of morphine and insist upon my using "pentothal."

I admire Dr. Brady's use of nitrous oxide in conjunction with "pentothal." In all my "pentothal" anesthetics of any length I use it and feel no compunction about switching agents just as if I were playing a musical instrument. I can produce beautiful balance by changing from one anesthetic to another. I like "pentothal" in conjunction with curare. I have used curare and "pentothal" in a few abdominal operations that were highly selected. I also use "pentothal" and curare in certain endotracheal anesthesias. I find it quite easy to get the catheter in place, and it is certainly much more pleasant to the patient to put him to sleep with "pentothal" for an intubation.

Dr. Fred E. Woodson, Tulsa, Okla.—I would like for Dr. Wright to say something about curare and "pentothal." Many men who use "pentothal," have some kind of apparatus to administer it in low dilutions. The dilution in the drip is usually glucose or saline, and it is run very slowly to keep the needle open and wash in the "pentothal." "Pentothal" is then given intermittently, as is needed to keep the patient asleep and relaxed. Occasionally curare is added to improve the relaxation. I have noticed in the little visible adapter on the needle that when curare is given, there is a visible precipitate. Nothing apparently happens to the patient, but the first time I noticed it, it alarmed me, and I discontinued the curare.

While in Miami, I talked to Dr. Wright, of the Squibb Company, who had a very good explanation of what takes place. I should like for Dr. Wright to tell you what happens to the precipitated "pentothal" and curare in the blood stream.

Dr. Lewis H. Wright, New York, N. Y.—The precipitate that forms when curare, which is slightly acid, and "pentothal," which is slightly alkaline, are mixed is barbituric acid. If an excess of the alkaline barbiturate solution is added the precipitate will dissolve. No harm comes from using the precipitated solution, for the

precipitate immediately dissolves when injected into the alkaline blood stream. If the precipitated material is allowed to stand and settle for some time there might be some change in potency due to the settling out of the barbituric acid. Most anesthetists prefer to use "pentothal" and curare through a three way setup with curare, saline or dextrose solution, and "pentothal" so arranged that the "pentothal" or curare may be washed into the vein by the saline so they do not mix and precipitate. Two separate needles, or one of many other ways may be used if preferred.

Dr. Brady (closing).—Dr. Elliott talked about "pentothal" for tonsillectomies. Dr. Elliott, I have used "pentothal" in only two tonsillectomies. I discourage them under "pentothal," but in those cases had no trouble. One had a tracheal tube, the other just the nasal tube with nitrous oxide. The saving thing is to have the head down and keep the suction fairly active. As Dr. Holly mentioned, keep the patient deep enough so that he is not swallowing too much. In five of my cases out of one hundred, "pentothal" was used for induction for various reasons. I do not object to using "pentothal" for induction with any type of anesthetic. As a matter of fact, I like it. I think the reason I do not use it more often is that I am just too lazy to set it up.

I do not know anything about the spraying of the throat or nose before other types of anesthesia. Unless one were going to intubate the patient, I do not see much need for it.

Dr. Holly said that he did not see the reason for giving continuous drip. The best reason I can give him for using it is that one uses less "pentothal." The patient is burning up "pentothal" at all times, not just intermittently.

What happens when you are using the syringe technic? The patient begins to move a finger so I push on the plunger rather nervously and shoot in one or two c. c. of "pentothal," which is more than the patient needs; whereas, if it is given drop by drop, the patient does not get more than he needs. Of course, it is not an intermittent method, because it is flowing into the veins constantly. To cut down the amount of "pentothal" I turn the screw clamp down regulating the rate of drop to just an occasional drop. I have used 0.8 gram "pentothal" in a 2½ hour graft from the tibia to the forearm. Most of you know that that is not a large amount of "pentothal" to use for 2½ hours of anesthesia with nitrous oxide added.

Dr. Austin mentioned using "pentothal" with spinal. In one of my cases it was used to supplement a spinal, one of them was used to supplement a local, and one to supplement a brachial block, which did not give complete anesthesia. I do not like "nembutal" premedication, but I do like morphine, because it cuts down the amount of "pentothal" used. For a short procedure like a dilatation and curettage, or to open an abscess or cyst, if the patient wakes up with morphine in him, he is not in pain. The patient under a very light barbiturate with pain sometimes reacts and complains noisily. I like to put the morphine in to cut down the amount of pain after operation.

In only one case did I combine curare with "pentothal." I have used curare with cyclopropane mainly. If I am running anything in a drip and there is a little precipitate from the curare, I do not pay any attention. If there is a precipitate of my "pentothal," I do not give it. I discard it and make up fresh.

I was asked what objection there is to "pentothal" in a local as a supplement for thyroid. There are two dangers. One is that of a respiratory depression; the second is that a patient may get a laryngospasm. Thyroid patients get laryngospasms easily, and I do not like "pentothal" in such cases. I use a double morphine technic of premedication and usually try to do them under oxygen and nitrous oxide or if necessary, cyclopropane. I do not have any hesitation in using combined anesthesia. If I am using "pentothal" and nitrous and it is not enough, I use cyclopropane to get myself out of trouble. I do not feel that it is a failure to combine any agents which add to the comfort and safety of the patient and to the comfort of the surgeon who is doing the operation.

THE TREATMENT OF CERTAIN TYPES OF SCLERODERMA*

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and

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This paper will deal with the treatment of circumscribed scleroderma of the type producing bands and plaques and morphea guttata. This treatment consists of the use of fever therapy by means of hot water baths. We are confining this report to the two above-mentioned types of scleroderma because such therapy has not been successful in our hands with diffuse true scleroderma, as defined by Sellei,[1] and acrosclerosis.

Scleroderma has no known definite etiology. Many writers think it is due to a vasomotor disturbance and more than half of the recommended therapy is based on an attempt to improve the

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circulation to the skin.[2,3] The arterial sympathectomy of Leriche and the ramisection and ganglionectomy of Adson, O'Leary and Brown[4] are attempts in this direction. Duryee and Wright[5] reported on the use of acetyl-beta-methylcholine chloride ("mecholyl") iontophoresis in thirty-four patients with scleroderma and vasomotor disturbances. Of twenty-seven patients who received ten or more of these treatments, sixteen showed marked or moderate improvement and eleven were essentially unchanged. These two authors felt that the improvement was apparently due to an increased vascularity in the affected parts. They were favorably impressed with this method of therapy because "mecholyl" iontophoresis has also shown softening of untreated areas through vasodilatation in contradistinction to the use of ganglionectomy, where results are local and limited to the extremity operated upon.

Other groups of workers have approached this problem from the viewpoint of possible endocrine pathology and consider that the vasomotor disturbances and calcium imbalance which are present are due to dysfunction of the adrenal, pituitary, thyroid or parathyroid glands. Seale[6] felt that those sclerodermatous individuals evidencing dysfunction of one or more endocrine glands possessed an inherent, unstable vegetative constitution, which was the result of an abnormal neuro-endocrinological mechanism. Huisemann[7] said that scleroderma undoubtedly belonged to the category of disturbance of the endocrine glands, the latter being due to some infection of the sympathetic nervous system, which acted as a nutritive center for the glands and blood vessels. The thyroid gland has probably received more reports as a causative agent than any other, but when one considers all of the cases showing involvement of the endocrine glands together, it seems likely that there is a pluriglandular trouble in many of them.

Leriche, Jung and DeBakey[8] believed parathyroidectomy was indicated as a therapeutic procedure because of the following facts and observations: hypercalcemia is frequently found in certain forms of scleroderma; cutaneous changes clinically and histologically resembling scleroderma have been experimentally produced by injections of parathyroid extract; studies of the skin in certain forms of scleroderma show an abnormal increase of calcium content; skeletal changes are not infrequently encountered in scleroderma, demonstrating a disturbance in calcium metabolism and reflecting parathyroid dysfunction.

In a comprehensive review of the etiology of scleroderma, Boardman[9] calls attention to trauma of various sorts as preceding the onset in many cases. This factor seems to be the rule in circumscribed scleroderma. Also, a possible toxic origin has been ascribed to infectious foci, cancer of the bladder, pregnancy and lactation. Reports of many cases are published in which there is an underlying or preceding infectious disease. These include typhoid fever, rheumatism, pneumonia, pulmonary tuberculosis, scarlatina, measles, malaria, tonsillitis and syphilis.

Hutchinson[10] was the first to note changes in the blood vessels, especially in the capillaries, and since then Durham[11] has shown marked involvement of the blood vessels post mortem. The studies of King[12] and Caldwell and Mayo[13] in scleroderma with the histamine wheal, in which the triple response of Lewis was found to be absent, suggest impairment of blood flow due to disturbance in the small arterial vessels. Numerous authors have found scleroderma and Raynaud's disease combined and felt that an angiotrophoneurosis was present in both conditions. We also subscribe to the hypothesis that scleroderma is basically due to an underlying angiotrophoneurosis.

The histopathological changes of scleroderma, according to Ormsby and Montgomery,[14] include thinning of the epidermis; homogenization and compression of the collagenous fibers, which, although increased in number, are individually narrowed and poor in nuclei; atrophy of the subcutaneous tissue; obliterative changes in most of the blood vessels; remnants of sweat glands; absence of sebaceous glands.

In morphea there is, in addition, a perivascular infiltrate at the periphery of the lesion and

beneath the area of edema in the upper parts of the cutis, composed chiefly of lymphocytes. Obliterative blood vessel changes are not marked in the areas of the perivascular infiltrate. This marked inflammatory reaction about the blood vessels at the periphery of the lesion accounts, clinically, for the blue halo often seen surrounding the plaque.

It appears, therefore, in scleroderma that the vascular pathology, endarteritis and intimal thickening of the small arteries, decrease in the number of capillaries, the contracting fibrous subcutaneous tissues and the possibly increased sympathetic tone all tend to impair the circulation to the affected part.

In 1934 one of us (C. C. D.) treated a case of central nervous system syphilis with hot water baths. This patient also had a large plaque of morphea on the back. Follow-up examinations of this patient revealed a startling observation in that the sclerodermatous area was regressing and after a period of six months the sclerotic process had completely disappeared except for a residual pigmentation where a purplish halo one-quarter of an inch wide surrounded the original lesion plus mild atrophy over the site of the plaque. This result encouraged us to regard hot baths as a promising therapeutic measure in scleroderma, since we felt that the vascular dilatation and resultant improved circulation must have been the main factor in overcoming the basic angiotrophoneurosis. However, it was also felt that through this medium of raising the body temperature, the reticulo-endothelial system would stimulate the body's natural defense mechanism. Thus, if any toxic factors were present as etiological agents, their chances of suppression should be enhanced.

Since then we have tried hot baths on several cases of scleroderma, including the generalized or diffuse types, as well as with acrosclerosis. However, real success has been confined only to circumscribed scleroderma of the plaque and linear types and morphea guttata. Up to the present we have had complete regression of these types of lesions in three cases over a twelve-year period. However, we do want to say that in only one of these three cases were hot baths the only attempted therapeutic measure. Glandular extracts from the ovary, thyroid, pituitary and pancreas and a concentrated vitamin A and D preparation were tried first but little or no success was noted until fever therapy by means of hot baths was instituted.

Although fever therapy has been known to aid scleroderma through its dilatory effects on the peripheral circulation, its use, to our knowledge, has been confined to intravenous injections of typhoid vaccine. However, physiotherapeutic measures, including contrast baths, ordinary baking followed by massage and active and passive exercise, produced the outstanding symptomatic relief in the series of cases of scleroderma reported by O'Leary and Nomland.[15]

Our method of administering hot water baths can be utilized by the patient at his home and, thus, is inexpensive and can be easily carried out. The only equipment necessary is a bath water thermometer, which can generally be purchased from any large dairy, a clinical thermometer, a bathtub with hot, running water, two cotton and two woolen blankets, bath towel and an ice cap. However, one additional member of the family must render assistance at home for this method of therapy.

The technic for taking the hot baths consists of the following procedure: first, the bathroom should be warm and free from drafts. Enough warm water, at a temperature of 95° F. is placed in the bathtub to cover the patient's umbilicus when he is placed in a semi-reclining position. Gradually more hot water is added until it covers the patient's shoulders. A peak temperature of 105° F. of the water should be attained for the first bath. It is advisable to have the patient's oral temperature, pulse and respiration taken every five minutes. Usually there is no danger of cardiac failure or heat prostration, even when the pulse and respiration increase with the elevation in temperature, if the quality is strong and rhythm persistent. The patient is kept in the 105° F. bath water until his oral temperature maximum has been attained. This will vary between 101-102° F. Subsequent baths, which are given twice weekly, should have the water temperature gradually increased until a maximum of 112° F. has been reached. However,

the patient's temperature should not be allowed to rise above 105° F. before removing him from the bath, nor should the water temperature be allowed to regress during the course of the bath. It may be necessary to run some of the water from the tub, in order to keep the water level and temperature as desired. After the calculated bath and body temperatures have been attained, the patient is removed from the tub and quickly wrapped in cotton blankets which are covered by woolen blankets and put to bed. The temperature, pulse and respiration are then taken every five minutes until the temperature has definitely begun to drop; when this is established, the temperature, pulse and respiration are taken every thirty minutes until the temperature has receded to 100° F. Then, when the patient has ceased to perspire, he is dried well, rubbed with alcohol and given clean, dry bed clothing. It is best not to allow food or water while the temperature and pulse are high. For a period of two hours prior to the bath no food should be taken except dry toast and sweetened tea. However, a diet high in carbohydrates and sodium chloride should be taken for the day preceding and the day following each bath. The time required to complete the entire treatment is approximately three hours. It is advisable to administer the baths in the evening, so that on completion the patient may sleep for the following eight or ten hours.

The following are brief histories of two additional cases of morphea successfully cured by these hot baths:

Case 1.—A married, white woman, 18 years of age, had guttate morphea around the neck and marble-like bands and plaques on the right side of the chest, the right arm, the entire right breast, the right side of the abdomen and the inner side of the right thigh. The lesions had been present five years. She had had no previous treatment. Her physical examination otherwise was normal, although her blood pressure was only 105/70.

She was first given whole gland ovarian extract and liver injections, intramuscularly, thyroid extract, quinine tablets and a concentrate of vitamins A and D capsules orally.

After one month on this therapy, there was no appreciable improvement in the sclerodermatous process, so she was told how to take the hot baths twice weekly. The vitamins A and D capsules and ovarian extract injections were continued along with the hot baths.

After five months the induration had completely disappeared, although there was a mottled whiteness and hyperpigmentation. The patient, having taken no further hot baths, was seen one year later, and the only residue was a pale, brownish pigmentation at the sites of the previous lesions. There was absolutely no induration, which was most remarkable, especially when one realizes that the entire right breast was as hard as a stone when she first appeared in our office for treatment.

Case 2.—A white girl, age 7 years, presented a large patch of morphea, which involved the total area from just below the shoulder blades to the hips. This was bordered by a purplish line, which was enlarged at certain places to a breadth of one-quarter of an inch. The skin in the center had a lardaceous, slightly atrophic appearance. This girl was put on nothing but hot baths at home after the technic we have outlined. Definite improvement was noted after the third bath and the condition had disappeared completely in six months. An examination five years later showed no remains except a slight, superficial, wrinkling atrophy of the skin.

Case 3.—We should also like to report the case of a 68-year-old white woman, who came to our office this past month complaining of a pruritus of the head; however, in taking a routine history it was disclosed that she had developed several patches of morphea on the anterior right thigh at the age of 7 years. In 1886 she went to Chicago to see Dr. James Nevins Hyde, who made a diagnosis of morphea and, in addition to recommending rest and large doses of cod liver oil, advised the use of warm saline baths. The plaques cleared on this regime in one year except for a residual brown pigmentation and slight atrophy; however, the interesting point to us was that the pigmentation still remained throughout this period of sixty years, which is the oldest case of morphea we have ever observed.

This last case illustrates, we believe, the value of warm baths and inclines us to believe that heat therapy has probably been considered as a treatment for scleroderma for many, many years, although it is doubtful that the high water temperatures we advocated have been extensively used.

We feel that the hot bath method has the advantage over intravenous typhoid or the electrical heat cabinet in the treatment of scleroderma in that the hot water comes in direct contact with the skin; whereas, in the fever cabinet a layer of air would prevent the skin from direct contact with the maximum heat and with intravenous typhoid the vascular bed of skin would probably not be dilated as much as with hot baths. Brown and Adson[16] at the Mayo Clinic have shown, through temperature measurements with the thermocouple cuff of the electro-

thermometer, that skin temperatures in the extremities normally rise 2-4° F. higher than oral temperatures when fever is present. This would tend to bear out our belief that hot baths would raise the skin temperature several degrees higher than the oral temperature, which is the basis for the use of this type of treatment in morphea.

In conclusion, we feel that the hot water bath method is the most successful one therapeutic measure we have employed for circumscribed scleroderma and we believe that its use should be much more extensively advocated.

SUMMARY

(1) The technic of hot water bath therapy for circumscribed scleroderma and morphea guttata is discussed.

(2) The rationale for this type of treatment is assumed to be due to the vasodilatory effects of high temperatures.

(3) Three cases are reported that have been successfully treated by this method, and we feel that its use is definitely indicated in the therapy of these two conditions.

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DISCUSSION (*Abstract*)

Dr. Wiley M. Sams, Miami, Fla.—Dr. Morgan has given us an excellent review on the etiology of circumscribed scleroderma and related disturbances, which serves to illustrate our paucity of exact knowledge of the disorders under discussion. If our information regarding these disturbances is slight, it is certainly matched, in most cases, by our lack of therapeutic effort. It has been my experience that the majority of our patients sense our feeling of futility, because we offer them no positive suggestions, and consequently they remain with us but a short time. Having consulted their family physician, and perhaps an internist, and then a skin specialist, they gravitate into the hands of an irregular practitioner of some description, whose therapeutic ingenuity far exceeds his scientific knowledge and his clinical acumen. In spite of this, he gives our disgusted patient something which we fail to appreciate, namely, a sense of well being because something is being done, and secondly, hope and encouragement, which are necessary for a recovery from any protracted illness. Drs. Dennie and Morgan are to be congratulated on bringing us a therapeutic suggestion which may be carried out by the patient with a chronic illness, without entailing too great a financial outlay, and one which offers a definite chance for bringing about definite objective improvement.

It is interesting to note that they cite scientific reasons for the superiority of water baths over other forms of fever therapy, in the treatment of cutaneous lesions. Perhaps there is a wider field of application for this form of physical therapy than we have as yet appreciated. Dr. Dennie's alert, clinical observation has brought us a therapeutic suggestion of value in an essential chronic disorder.

Dr. Paul Power, Waco, Texas.—I want to ask, is the bathtub covered during the baths?

Dr. Morgan (closing).—It does not have to be. I think, if the room, as we said, is warm and free from drafts, that will not be necessary. We have done much of this work at the Mercy Children's Hospital in Kansas City on congenital syphilis. At first the top of the bathtub was covered with canvas except a place for the head, but we have found that as long as the body temperature can be elevated, that is the most important thing and it can be done without covering the tub.

Dr. Erich Brockelman, St. Louis, Mo.—How do dry, hot applications do?

Dr. Morgan.—We have not attempted dry heat locally. At present we have a young boy, about six years of age, who has a patch of morphea on the left cheek in front of the ear, and we have tried using hot,

wet packs locally to the area. I saw him about two weeks ago, after four months of such daily applications, but they have not been successful. So, I feel that if we are going to arrive at any success with hot water treatment, we will have to use the hot bath. I do not know whether it will work on lesions of the face or scalp, where the involved tissues cannot come in direct contact with the hot water, but from the neck down, where the hot water can come in contact, I feel sure that over a prolonged period of time, satisfactory results in the majority of cases of this type can be obtained.

Dr. J. R. Allison, Columbia, S. C.—Have you tried it on generalized scleroderma? Do you think it would be advisable?

Dr. Morgan.—Dr. Dennie has tried a few cases, and apparently it is not successful in the generalized type but only in the circumscribed types of morphea guttata. Nor do I think it works too well on acrosclerosis. We have such a case in a girl now we are trying on this technic. Her hands seem to have shown some improvement, but I do not believe we are going to get a completely satisfactory result, as we did in these other types.

Incidentally, we have a girl with Raynaud's disease, who began using this method of treatment in 1940. At that time, after three or four months, she obtained complete regression of this condition, but each fall it has returned. At such times she begins taking hot baths twice a week. After two to three weeks she obtains enough relief from the symptoms for the remainder of the cold weather, until the following year.

There is just one other point I should like to bring out, which I did not mention in the paper. When a patient's temperature rises to 103,° it is advisable to check the temperature every two minutes, because sometimes further elevation occurs rather suddenly, and it is not desirable to have the patient's oral temperature much above 105° F.

THE TREATMENT OF STERILITY IN THE FEMALE*

By LEE J. GLOBER, M.D.
San Antonio, Texas

I wish to express my appreciation for the privilege of addressing this section again on a similar subject presented 10 years ago in New Orleans. Some progress has been made in the past decade; more might have been except for the recent holocaust. Until we have solved the problem of human reproduction, we have only for our aid the fringes of the solution to the problem of human sterile mating. By careful perfectionist type of study and utmost cooperation on the part of both husband and wife, we can offer at present a viable baby to 45-50 per cent of all sterile couples.

The importance of this problem cannot be overemphasized. There are estimated to be between 2 to 4 million childless couples. Meaker claims that 15 per cent of married couples are involuntarily sterile. The first chapter of Genesis tells us to "Be fruitful, and multiply and replenish the Earth." It has been said that the successful accomplishment of the reproductive function is the culmination or goal of woman's psychosexual maturity. Those who fail often experience disillusionment, emotional frustration with resultant conflicts in the stability of their homes and their proper position in society. Witness the indignation of childless women over the woman who complains of her ease in conceiving. There are no more grateful patients than the couples one has helped to make parents. The doctor may well bask in his part in contributing to the glory of new life.

The problem of sterility is complex. Note the frequency of the term sterile mating, for it rarely concerns one individual but deals with both husband and wife. The two essential partners possess relative degrees of fertility; the ability to correct the multiple factors may determine the success or failure in accomplishing a term pregnancy. A case is never accepted for study without the fullest cooperation of both.

I shall try to carry through by description, my routine in handling these patients: To be kept in mind at all times are the requirements as listed by Rock: ovulation, spermatization, insemination, conjugation, migration and nidation.

Every effort is made to make a detailed study from every phase, calling in consultants like the internist, genito-urologist, pathologist, etc., whenever necessary. A history is painstakingly obtained noting both partners' libido, frequency of sexual relationship, sexual technique, past history, especially of abortions and infections, family background of fertility, habits, diet and mental status of both partners. A pelvic examination of the outlet, vagina and cervix is made. Causes for dyspareunia, effluvium seminis, vag-

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inal and cervical infections, cervical mucous plugs, stenosis of cervix, malposition of cervix, cervical polyps; all these may reveal the failure in proper deposition, migration and interference with life of the spermatozoa. The uterus may reveal causes of sterility, namely: varying degrees of hypoplasia, myoma that may or may not interfere with fertility, infected polyps, malpositions, etc. A patient with endometriosis is very likely to be more sterile than the average sterile individual. The adnexa are noted for their pathology.

Unless we find the wife absolutely sterile, the husband's semen is examined. The specimen is obtained in a sterile jar, never by the condom method. A quick but fairly accurate estimation of the fertility of male semens can be ascertained by noting the number, viability and uniformity of sperm heads. A percentage of 85 per cent or above of uniform normal spermatozoa is usually a very fertile specimen, provided that proper liquifaction takes place within 20 minutes. If the specimen is not up to par, he is sent to an internist and genito-urologist.

A Hubner or postcoital test is done about the time of ovulation, for then the cervical secretions are most receptive to the deposited semen, recording whether or not the spermatozoa succeeded in migrating through the cervical canal. Cervicitis is handled by cautery, polyps are removed and the base cauterized, stenosis of cervix gently dilated by small calibre cervical dilations, all this handled at the office. After proper treatment, a repeat Hubner test is done to substantiate the success of our treatment. A precoital douche of Ringer's solution many times seems to assist in the viability of spermatozoa in the vaginal secretions of some women. Postural treatment and later checking oftentimes overcomes the malposition of the cervix that points up and out of the seminal pool deposited in the vagina.

The patency of the fallopian tubes are determined by the well known Rubin test. I prefer the flexible tip or short-tipped metal canula to prevent trauma of the cervical canal. I also prefer diodrast rather than lipiodol or the other heavier radio-opaque substances in uterosalpingographies. The pictures are excellent and it is painless and safe. The Rubin test may be therapeutic if the tubes are non-potent. Witness the success in some cases where the test is done repeatedly until the tubes are finally made potent. This test does have its dangers and must be used with caution. Endometrial biopsies using the Randall curette is done in the first few hours of the menstrual period. Since not all so-called normal menstrual periods are ovulatory periods, it is necessary for us to determine whether or not the patient has normal premenstrual endometrium. The rest of our laboratory tests are basal metabolic determinations, Rh factor, complete blood counts and serology.

Now that we have listed all the diagnostic factors that produce our sterile couple, we then must eliminate or improve these plural factors; rarely is it one single factor. We have already discussed the treatment of the outlet, the vagina and the cervix. Mild doses of oral estrogen are cautiously given, sometimes if the cervical secretions still remain cloudy and thick.

It is essential that good general hygiene should supplement specific attention to the generative tract. Good physical condition promotes good breeding conditions. Such age-old advice as proper exercise, rest and diet is carefully and specifically given. The tempo of the mode of living may have to be changed. Additional vitamins or mineral therapy may be necessary, or a changed diet to include more proteins, fruits or vegetables. Additional thyroid for the hypothyroids to the normal threshold is one of the most important adjuncts to our present therapy. Psychosomatic influences may bear much importance, and correction here is of value. Infrequent or too frequent sexual congress without proper sexual technique, like using lubricants or going to the bathroom immediately after the sexual act, sometimes produces an issue after advise is given.

I believe that the use of the morning basal temperatures in determining when ovulation occurs is of value to the intelligent, emotionally stable women. For the frantic wives and most of them are that way, I usually advise concentration during that week of 14-16 days before the next expected menstrual period. I try to lessen their anxiety and help their mental state by advising them that if all instructions are

carried out, a pregnancy may eventually ensue, if they can stop living from one menstrual period to another.

To date, I have not much faith in any additional high powered hormonal therapy to produce ovulation. It is expensive and the failure is nerve-racking to both doctor and patient. I wonder if the very small percentage of successes might not have happened if no specialized organotherapy had been employed. I do confess that I have sometimes succumbed to the patient's pleas for these hormone shots, only to be further convinced that to date we are only muddling with our efforts to produce ovulation by these shots.

One sees numerous operations performed on these unlucky women that are unnecessary and often produce permanent sterility. Surgery should never be contemplated unless every other factor permits a fertile mating. The uterus in malposition rarely if ever has to be corrected by surgery. Most dilations of the cervix can be accomplished with relatively little discomfort in the office. Myomectomies and plastic surgery to the tubes and ovaries are done in very selected cases, but only after advising the husband and wife as to the small incidence resulting of pregnancies even though the operation be a success. To me, the resulting pregnancies are worth the other failures; but surgery performed without other careful investigation and honest presentation as to their chances to the patient, is to be condemned.

Spontaneous abortions in the early stages are a form of relative infertility. Rock has shown that 40 per cent of all his early fertilized human ova start off wrong and would abort regardless of what treatment was given these patients. Judicious use of rest and synergistic doses of both corpus luteum hormone and estrogen will reduce the incidence of abortions of the normal embryo. Further investigation may reveal in the future the problem of producing normal human ova and normal development of that ova.

Artificial insemination is sometimes used where the husband has a permanent complete absence of spermatozoa. I do not encourage it and will only use this measure if I feel reasonably sure that the wife is fertile and the husband is enthusiastic about the use of an artificial donor. The technique is simple, just depositing the semen in the vagina with the cervix dipping into the seminal pool formed. The cycle of ovulation is found to determine when the inseminations are to be performed. I use three inseminations per month and using a different donor per each insemination, so that the potential sire of the pregnancy produced is thus relatively unknown. The advantages of artificial insemination over adopting a baby are two: the child produced may be better endowed than the baby adopted; second, it gives the wife the privilege of carrying out her normal desires and function of conceiving and carrying through with a full term pregnancy.

In conclusion, let us again repeat the inadequacies of our present knowledge of the problem of sterility; that each sterile mating be given the advantage in detail of our present diagnostic and therapeutic measures; and to look in the future to contributions from further investigation of our endocrinologists, pathologists, surgeons, chemico-physiologists, sociologists, psychiatrists, and even fields not known to date—that we clinicians can hope to increase our incidence of success in this important problem, the problem of sterile mating.

DISCUSSION (*Abstract*)

Dr. Gilbert F. Douglas, Birmingham, Ala.—It is my feeling that it is going to be a long time before artificial donors are generally accepted, certainly in certain sections of the country. In our section it will be taboo for some time on account of the question of legality, some might question the morality, and then, I think because of the timidity of those who are doing sterility study we may be rather slow to take up and use artificial donors.

We should not rely much upon surgical procedures. If we expect to accomplish much with these patients, it is going to be based largely upon the meticulous care that is used in diagnosis. If we are able to find the minor points which are the causes of sterility, we shall accomplish a great deal. There is no doubt that the anovulatory condition plays a very great part in this, and before going into treatment, we should know as far as possible whether the patient is ovulating. This, as he has stated, is best determined on the first day of menstruation by obtaining endometrial biopsies.

Secondly, before we go too far into the case, the husband should be brought in and given his part of the study. If we get husband and wife as partners from

the beginning, we shall accomplish more. If we attempt to do our study on the wife, allowing the husband to escape for some time, it is very difficult ever to get him in. If we can get them to come together the first time to start this study, we shall get better results.

Dr. Glober has a high percentage, 40 to 50 per cent, of success. That probably is higher than most of ours.

Dr. James R. Bloss, Huntington, W. Va.—Glober mentions the endocrine study of the female. Nothing has been said about an endocrine investigation of the husband. Just because a man is able to accomplish intercourse, he thinks there could not possibly be anything wrong with him, yet, even though he has living spermatozoa, they lack something. Some eight or nine years ago when I was Chairman of the Obstetric Section, I begged and pleaded for routine metabolic tests for all pregnant women. A few men have been doing that in the country since that time. I have yet, after eight years, failed to find an anatomic abnormality in a child in which one or the other or both of the parents was not a hypothyroid. Just recently I had a patient who was perfectly normal, other than being a marked hypothyroid case, and yet we find an absent fibula in a child. In absent bones, harelip, cleft palate, and anencephaly, you will find one or both parents are hypothyroid.

In many sterility studies we should not depend upon an endocrine investigation of the mother alone. The father may be a hypothyroid with defective spermatozoa. There is yet much to learn in this field.

I am questioning very seriously how much we should go into a tailspin, so to speak, over this minus Rh. I do not know. The evidence is confusing to say the least. Hunt presented a paper in September, before the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, in which he said that more of his Rh positives aborted than had the Rh negatives. He had not run metabolic tests upon either the positives that aborted, or the negatives.

I can recall cases in which a childless couple have adopted a child and in less than a year and a half or two years, the woman has become pregnant. For those of you who might be interested in psychiatry, there was a paper published not too long ago in which the author gave an explanation of why after adopting a child the woman became pregnant. It is his idea that it was due to the effect upon the pituitary gland of gratified maternal instinct and that then she begins to ovulate.

At the present time we are watching the ovulation rhythm and predicting the period of ovulation by watching the temperature. We have a case in which we feel that probably anticipating the ovulation period, by correcting the endocrine dysfunction, the woman has become pregnant.

Dr. M. Y. Dabney, Birmingham, Ala.—Various reasons occur why apparently normal couples judged from routine work-ups of husband and wife, do not have children; and they are difficult to determine. For example, iodized oil may be clearly seen passing from both tubes at a normal pressure. Yet the Rubin test may be negative. Such a case may be tricky in that there are numerous old adhesions binding the omentum and intestines together and about the tubes. Both oil and gas that are forced through the tubes may be distributed within the folds of the intestine and omentum and in no way communicate directly with the ovaries.

Another pitfall is a poor reading of the endometrial biopsy although it may have been taken within the first twelve hours of menstruation and may show a progestin reaction, but really representing only the eighteenth or twentieth day of the cycle in its development, which means a poor bed for nidation of the fertilized ovum. Such a case with proper treatment stands an excellent chance of being reclaimed, but without treatment may continue infertile.

More papers on sterility should be read at meetings, because this is the least generally understood subject in gynecology and obstetrics in proportion to the frequency of infertile marriages. Those engaged in the work should spread the new information that constantly is being discovered.

Dr. S. P. Smiseth, St. Petersburg, Fla.—I obtain spermatozoa from the vagina, put a hanging drop in the back of the hemothermometer and examine it in the microscope. It takes about one minute, and the husband is taken care of without the disagreeableness of appearing in the office.

I think that testosterone will increase the fertility of the male, and the luteinizing *sinapoidin* will increase the fertility of the female in the same way.

Dr. Glober (closing).—I believe that it is very important to take the basal metabolism of both the husband and wife, both in the treatment of sterility and in habitual abortion cases. Thyroid does no good to those patients who have a normal basal metabolism; it is only of value to the hypothyroid patient.

I have used semen from a husband of low fertility as a donor in artificial insemination, hoping thereby to assist the sperm in getting into the uterine cavity. My success has been very poor. Sometimes I wonder if that husband should be allowed to be the father of a baby, if his sperm count is not up to normal. It is possible that we may get a larger percentage of freak babies, unless the semen is good.

Most of my office patients know that I will not accept them unless their husbands will cooperate. I therefore have no difficulty in getting the specimen in a sterile jar. We get the specimen by two methods: either by masturbation, which I prefer (and that, of course, is done at home) or the other method is the withdrawal method, using the wife and then getting the specimen in the jar. I believe that you will get a more uniformly accurate estimation of the specimen that way, than by getting it from the vagina. Many a patient comes to the office with most of the specimen already lost, and the examination has to be repeated.

KRUKENBERG TUMOR, PRIMARY*

FOLLOW-UP REPORT

By C. J. ANDREWS, M.D.
Norfolk, Virginia

The main facts regarding Krukenberg tumor of the ovary have been widely studied and for the most part agreed upon. This tumor was first described by Krukenberg in 1896. The description, gross and microscopic, which he gave still stands to identify it. They are solid tumors usually of moderate size and almost always bilateral. The surface is smooth usually, but not always free of adhesions. The contour corresponds to that of the ovary. The weight of the tumor is most striking and will suggest this tumor to the operator if this characteristic has been thought of.

Many excellent descriptions of the microscopic appearance of these tumors have been published. The most characteristic single element is the signet ring cell which is produced by mucus distending the cell and shoving the nucleus to one side. Some have observed tumors which were characteristic otherwise and were considered to be Krukenberg which did not show the signet ring cell. Krukenberg believed these tumors to be primary although in some of his cases he observed cancer in other viscera. He also believed them to be connective tissue tumors. Subsequent study showed them to be carcinoma. It is now agreed that they are nearly always secondary to some growth elsewhere either in the alimentary canal, breast, or gallbladder. So usual is this finding that it has been believed to be exclusively a secondary tumor.

In 1933, I reported before this section three cases of Krukenberg tumor. In one case I could find no primary tumor outside of the ovary and suggested that it might be a primary Krukenberg tumor of the ovary. These slides were later examined by Dr. Emil Novak who agreed that it fulfilled all the requirements for the diagnosis of Krukenberg tumor. Dr. Novak was also kind enough to examine this patient and he could find no evidence of any other primary growth. When my report was made the patient had been operated upon only about four months previously and we were still fearful of development of the process in some other location. This patient was examined September, 1946, and no evidence of the disease has yet occurred.

Following are the original notes on this case:

"A woman of 50 years had been married 12 years with no pregnancies. Her chief complaint was of pain and a feeling of pressure in the pelvis, with urinary frequency and a dull ache over the left kidney during the preceding several years, which had become progressively worse during the previous three months. Her periods were normal until six months before examination, and she had not menstruated since that time. There was no history of digestive disturbance. The pelvis contained a mass about the size of an orange.

"She was operated upon May 11, 1933. The pelvic mass was found to be globular and firm in consistency. It was attached to the bladder and other pelvic structures by adhesions. When isolated it was found to be a tumor of the left ovary. The uterus was normal and displaced to the right. The tubes were normal. The right ovary contained a small hemorrhagic cyst. A bilateral salpingo-oophorectomy and supravaginal hysterectomy were done. A small indurated gland was palpated near the pylorus of the stomach, but otherwise the abdomen was negative. A frozen section of the ovary specimen was reported as adenocarcinoma. Later slides showed some areas containing signet ring cells.

"The pathological report, made by Dr. L. J. Motyca, Pathologist at the Norfolk General Hospital, follows: The left ovary is 70 mm. in diameter. It is almost large as a baseball. It is hard and nodular. The cut surface is grayish-white in color with extensive necrosis. The necrotic areas are yellow in color. The right ovary is 30 x 25 x 12 mm. It is rather small and contains a small hemorrhagic cyst. On microscopic examination, the section of the right ovary contains a small group of alveolar glands which are lined with ciliated columnar epithelium. The wall of these cysts contains large phagocytic cells which are filled with hemosiderin. These indicate old hemorrhage. The diagnosis is endometriosis of the right ovary. Microscopic examination of the left ovary shows no normal ovarian structures in any of the sections. The bulk of the tissue is composed of single or small groups of large round or polyhedral cells, scattered in a field of connective tissue which is chiefly of the mucoid type. Most of the tumor cells contain large droplets of mucus which have pushed the nuclei to one side in a signet ring form. They are intimately associated with the mucoid connective tissue stroma. The cells of the latter are either stellate or fusiform. One section shows a second type of epithelial tumor which is distinctly alveolar. The alveoli are moderately large and they are lined with one or more layers of columnar epithelium. The epithelial cells stain deeply with hematoxylin, and many of them contain small droplets of

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mucus. The alveoli form a distinctly minor part of the tumor. Some portions of the tumor have undergone coagulation necrosis. Others contain a moderate infiltration of lymphocytes.

"The diagnosis is Krukenberg tumor.

"In the uterus there is no evidence of malignancy. A uterine polyp contains cystic glands which are lined with low columnar epithelium. This is surrounded by edematous stroma. The endometrium also contains cystic glands which are small in size. The diagnosis is benign polypoid lymphoplasm.

"On May 27, 1933, 16 days after the operation, an x-ray study of the gastro-intestinal tract was made. No abnormality was demonstrated. On September 21, 1933, this patient was examined by Dr. Emil Novak, who also had x-ray made of the chest, heart and gastro-intestinal tract. The reports were negative except for spastic colon. She continues to be free of any symptom of the disease."

A similar case was reported in 1920 by Frankl whose patient was well 3¼ years after removal of both ovaries. Here there were no gastro-intestinal symptoms and negative x-ray findings.

A less typical case was reported by Newmann. A tumor growth recurred in the pelvis seven years later. Palliative x-ray was given. The patient was still living and in comparatively good health 9 years later. No gastro-intestinal symptoms had developed.

Apparently there is still some doubt as to the existence of primary Krukenberg tumor. When my case was known to have been living and well 4 years after operation, Jarcho expressed the opinion that,

"As more and more care is devoted to the study of individual cases, the proportion of instances meriting inclusion under the rubric of primary Krukenberg tumor will steadily approach zero."

The question of the existence of a primary Krukenberg tumor has some practical significance. Since secondary Krukenberg tumor is practically always fatal and the primary growth may not be, this would be of much interest to the individual in whom the diagnosis of primary growth was justified. Krukenberg tumor is thought to be a rather rare occurrence. About 300 cases have been recognized and of these, not more than 3 are believed to be primary.

The fact that this case has lived 13 years without development of symptoms is very strong, if not conclusive, evidence that there is none now and never has been any growth here outside of the pelvis. Of course, cancer may be of very slow growth and might still develop but the prospects of this seem so remote that one would seem justified in concluding that this was a primary Krukenberg tumor.

DISCUSSION (*Abstract*)

Dr. Hudnall H. Ware, Jr., Richmond, Va.—Naturally, one questions the diagnosis in a case like this, in which there are apparently only two cases reported in this country where there has not been a malignant growth in some other part of the body. Dr. Novak in his book reports this case so that the diagnosis is made not by one pathologist but by several persons.

Dr. Robert T. Spicer, Miami, Fla.—A point worth stressing is the inter-relationship of pathology seen in various parts of the body. As in the case of the Krukenberg tumor, a solid tumor may be primary in the pelvis or secondary to gastric or other primary growths.

Often specialists think only in terms of their own special field. One of the lessons from this presentation is that, as gynecologists and obstetricians, we have to consider the patient as a whole and to look for remote sources of trouble in the pelvis. Then, when only a rare diagnosis is possible, we may be pleasantly justified in knowing that there have been such rare entities as primary Krukenberg tumors. Thus if a rare answer should be predicated elsewhere, we may have an alibi.

OBSERVATIONS ON THE USE OF "DEMEROL"*

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Morphine undoubtedly takes first place in the list of remedies used for relief of pain. Even with this realization, most physicians acknowledge that morphine has certain side actions which are undesirable and in certain instances highly dangerous. The differential between the therapeutic and toxic dose is usually small. There is definite danger of addiction in long continued use and depressing effects are frequently encountered. The action of morphine on the smooth muscle at times is not desired. Thus a continued search for a drug with the analgesic properties of morphine less certain of its side action is desirable. I do not feel that "demerol" meets all of these specifications but it is a drug with valuable analgesic sedative properties and a low index of toxicity.

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"Demerol," chemically 1 methyl 4 phenyl piperidine 4 carboxylic acid ethyl ester hydrochloride was synthesized in 1939 by Eisleb and Schaumann. It has been accepted by the Council of Pharmacy and Chemistry for inclusion in "New and Non-official Remedies" as meperidine hydrochloride.[1] Chemically it is more closely related to atropine then it is to morphine. An unexpected finding was that the drug had morphine-like analgesic properties on the central nervous system. It has pharmacological properties which are common to atropine, papaverine and morphine.[2] Following prolonged administration to animals no deleterious effects were noted in the blood producing organs, liver, spleen, stomach or bone at necropsy.[3]

Three main actions of "demerol" may be considered, namely: analgesia, spasmolysis and sedation.

Analgesia.—The dose of "demerol" is 50-150 mg. given orally or intramuscularly, with 100 mg. an average effective dose. In very severe pain it may be given in doses of 150-200 mg. without toxic effects. Any increase in single doses beyond this is of no value and these higher doses are not usually given. Given orally, the effect is felt in fifteen minutes, reaches a peak in one hour and persists to some extent up to six hours. Given intramuscularly the effect appears in five to ten minutes and persists for three to six hours. It has been fairly well established that 100 mg. of "demerol" is about equal in analgesic value to 10 mg. (1/6 grain) of morphine. The duration of action of "demerol" is slightly shorter than is that of morphine. Fifty mg. of "demerol" is slightly superior in value to 30 mg. of codeine. It appears that visceral pain, that is, pain from the pleura, peritoneum and smooth muscle is more effectively relieved than is pain arising in the skeletal muscle and neurological structures.[4] "Demerol" may be administered intravenously, but should be given slowly by this route. As the effect of the drug is felt quite promptly following intramuscular administration there would appear to be little practical use for this channel.

Spasmolysis.—In direct contrast to the action of opiates, the mobility of the intestines is so influenced that the segmental contractions and tone are diminished while the propulsive action is unaltered. This would materially aid in the relief of colicky pain. It has been found that "demerol" has an antispasmodic action on the intact ureter.[6] Studies on intact and excised uteri have given variable results.

Sedation.—This is usually light and results when larger parenteral doses are given. This effect usually subsides within a period of two or three hours, but may last longer when the drug is given at night. If sleep is induced, there are no after effects or "hang over" when consciousness returns. The sedative action is seldom sufficiently pronounced to militate against the use of the drug even in ambulatory patients. Obviously in many conditions the sedative effect is desirable. I have had a patient who noted a marked decrease in sexual desire while taking "demerol." Wieder[25] mentions this observation in patients 1 and 3 in his report.

CLINICAL USE

(1) *Cardiac Conditions.*—In pain due to myocardial infarction the drug is of value, but I do not feel that it replaces morphine. It is of definite value in an elderly patient in whom it is particularly desirable to avoid respiratory depression. Doses of 100-150 mg. may be given and repeated in two to three hours. I have alternated it with morphine in this condition. I have also found the drug of value in paroxysmal dyspnea due to congestive heart failure.

Curry[7] mentions an interesting point regarding its use in myocardial infarction. Because of negligible respiratory depression venous return to the heart is favored thus decreasing the stasis of blood in the legs, phlebothrombosis and subsequent pulmonary embolism.

(2) *Broncho-pulmonary-pleural Conditions.*—Asthmatic attacks may be benefited by virtue of the antispasmodic and analgesic effects of "demerol." It may well be combined with epinephrine and given in the same syringe. Small doses of each drug, for example 30-50 mg. of "demerol" and 0.2-0.3 c.c. of epinephrine may be helpful. This dose may be repeated at frequent intervals if necessary. "Demerol" may also be combined with ephedrine in capsules for oral administration. As morphine is generally contraindicated in asthma, "demerol" may also aid by allaying the fear component which is frequently present in severe attacks. In pain of pleural

origin the drug is of value. Some of the distressing symptoms of pneumonia may be relieved by the analgesia-sedative effect of "demerol." However, tracheo-bronchial irritation and cough are not relieved by the drug.

Waterman[8] has used "demerol" in approximately twenty-five patients undergoing thoracoplasty. He has used it combined with scopolamine for preoperative sedation. He has also used the preparation postoperatively, obtaining satisfactory relief of pain and no undue respiratory depression. He feels that the drug is particularly valuable in patients with poor respiratory reserve.

(3) *Pain of Smooth Muscle Origin.*—There is considerable evidence accumulating that "demerol" is at least or even more effective than is morphine in the relief of intestinal, renal, and biliary colic. This is partly due to the potent antispasmodic action as well as the central analgesic action. Relaxation of smooth muscle spasm whether gastro-intestinal, renal or biliary can frequently be obtained within ten minutes after administration of 100 mg. intramuscularly.

(4) *Surgical Conditions.*—Batterman,[9] Weinstein,[10] and White,[11] claim that highly satisfactory results were obtained in a group of patients treated postoperatively. Good pain relief was obtained and there were few untoward reactions.

(5) *Obstetrical Use.*—Several observers have reported on the effect of the drug in obstetrical analgesia.[12 13 14 15] Schumann[13] reporting a large series of patients says that in conjunction with scopolamine, "demerol" is superior to other drugs in common use.

(6) *Other Conditions.*—"Demerol" has also been of use for the relief of pain in thrombosis of peripheral arteries, acute and chronic arthritis,[16 17] various types of neuritis, migraine, tabetic crises,[17] and multiple sclerosis. It is useful to control pain following certain diagnostic procedures as cystoscopy, retrograde pyelography, gastroscopy and bronchoscopy. I have found it useful in the symptomatic relief of chronic headaches until more definitive programs can be established. It is useful for initial analgesia of peptic ulcer therapy. In dysmenorrhea it gives effective relief and a few doses may suffice to control the pain of that particular period. It is not effective for relief of pain in acute rheumatic fever.[16]

In far advanced painful, malignant conditions, it has proven useful for relieving pain. There is no necessity for considering addiction in such a situation but continued use here may avoid some of the unpleasant side actions associated with the use of morphine. In addition, morphine may be used as a supplement or terminally.

Heldt[18] has used the drug to decrease the discomfort incident to artificial fever therapy produced by the hypertherm. They suggest further investigation of its use as a sedative-analgesic in other types of fever.

(7) *"Demerol" as a Preanesthetic Agent.*—Rovenstine and Batterman[19] found 100 mg. "demerol" and 0.6 mg. scopolamine satisfactory for preanesthetic medication. Respiratory depression occurred in 3 per cent of the series.

SIDE EFFECTS AND TOXIC EFFECTS

Certain unwanted side effects may occur with therapeutic doses of the drug. Those seen most frequently are dizziness, nausea and vomiting. The percentage was considerably higher in ambulatory patients. With prolonged administration of the drug, side effects occur much less frequently. Severe reactions are rare and take the form of severe weakness, pallor, syncope, clammy perspiration, dizziness, nausea and vomiting. As "demerol" is a vasodilator, this response is probably related to an inability to maintain the circulatory balance when the patient is ambulatory. Assumption of the recumbent position for fifteen to thirty minutes usually lessens or aborts unpleasant side effects. Respiratory depression is rarely seen in the average patient; however, Guttman,[20] of the Neurological Institute in New York, cautions against the use of the drug in patients with intracranial lesions.

ADDICTION

Any drug which possesses a morphine-like action must be considered from the standpoint of producing physical dependence or addiction. "Demerol" can produce physical dependence. This had been shown in experimental work on former morphine addicts, but apparently it has not been easy to produce addiction to "demerol" even in these patients.[3] "Demerol" might be

expected to produce addiction in certain unstable persons who would abuse an opiate in continued administration. It might be expected to produce addiction in a psychically stable person requiring administration of a strong analgesic over a prolonged length of time. So far, there is little evidence that addiction has occurred in the latter group. Habituation or a desire for the drug minus physical dependence is also a possibility which should be noted.

In June, 1946, De Kruif[21] published in *Reader's Digest* an over-enthusiastic article upon "demerol." This made extravagant claims regarding the efficacy of the drug and also minimized its addiction liability. This type of report certainly does not do the reader or the drug any good service. Mr. H. J. Anslinger[22] of the Federal Bureau of Narcotics took cognizance of this report and outlined briefly fifteen case histories involving "demerol" addiction. Apparently seven of these are primary addictions to "demerol" and did not involve other narcotics.

Schneck,[23] reported an early case of "demerol" addiction. However, this patient had prior experience with narcotics.

Samter[24] mentions that in Germany more cases of addiction to "demerol" are being recognized.

Wieder[25] says that numerous patients have been admitted to the United States Public Health Service Hospital at Lexington, Kentucky, because of "demerol" addiction and cites three case records in fair detail. Each of these patients developed a marked tolerance to the drug and a high degree of euphoria and made strenuous efforts to continue use of "demerol." One patient said that he preferred the effects of "demerol" to those of morphine. Wieder concludes that "demerol" is an addicting drug and the same precautions should be observed in its use as in the use of opiates.

Physicians who have occasion to study patients with "demerol" addiction should certainly review their cases in the medical literature. Attention should be paid to ease of addiction, personality of the patient, withdrawal symptoms, frequency of relapse and other pertinent findings relating to physical dependence. These histories would be of particular value in individuals who had no prior experience or addiction with any opium derivative. Considering the evidence available at present it does not appear that addiction is likely to occur if the physician keeps within the bounds of the usual medical indications for the drug. I would feel that the greatest danger of addiction is in individuals with an unstable psyche and certainly great caution should be used in administering this or any other potentially habit forming drug to this group of patients.

In no patient of mine have I seen any sign of physical dependence or any withdrawal symptoms when ceasing medication.

SUMMARY

Evaluation of any analgesic is somewhat difficult as one is mostly dependent upon subjective statements as to the preparation's ability to relieve pain. "Demerol," as synthetic analgesic-antispasmodic and sedative agent, shows sufficient promise to merit further investigation and clinical use.

Toxic actions of the drug are slight, unpleasant side actions are usually mild and respiratory depression is uncommon.

The possibility of physical dependence is present and should be kept in mind when the drug is given during a long period of time.

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NEAR ELECTROCUTION AS A CAUSE FOR PROTRUSION OF AN INTERVERTEBRAL DISC: CASE REPORT*

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Voluminous literature over the past several years testifies to the increasing importance of the intervertebral discs. The pioneer work of Schmorl[1] has given impetus to the study of the special pathology of these structures. Herein is contained the study of a case of protruded lumbar intervertebral disc apparently due to electrical shock and a search of the literature upon the disc syndrome with particular emphasis on etiology.

The intervertebral disc itself can be considered as being composed of three parts; the cartilaginous plates enclosing it above and below, the nucleus pulposus, and the annulus fibrosus. The disc proper consists of the annulus fibrosus, a fibrocartilaginous ring which surrounds a central collection of gelatinous substance, the nucleus pulposus.[2]

The chief forces to be withstood by the human spine are two: pressure, mostly intermittent in the form of mechanical shock in a vertical direction, acting upon the broad surfaces of the vertebrae and distributed by the spring-like nucleus pulposus.[3] The second force is the result of flexion and torsion, the burden of which is carried by the annulus fibrosus.[2] Because of its embryologic formation the annulus fibrosus is weakest at its point of embryologic fusion in the midline posteriorly. The posterior longitudinal ligament, thickest in the midline, forces the protrusion laterally. Consequently, most of the protrusions are found in this region.[4] The protrusions of the nucleus pulposus, therefore, are based upon an embryologic defect. Degenerative changes or trauma may precipitate the pathology.[5] Moreover, repeated minimal shocks definitely weaken the annulus fibrosus and thus predispose the intervertebral disc to protrusion in the presence of a precipitating injury.[6] The trauma may be relatively mild or it may be more violent and severe. Most often it is sudden. Commonest causes include falls, compression in accidents with or without compression fractures of the vertebrae, lifting of weights, manipulation of the spine, and sudden jerky and powerful voluntary movements. The protrusion occurs with the spine in the position of flexion. This narrows the intervertebral space anteriorly and widens the space posteriorly. Thus upon the occasion of trauma, the compression force tending to displace the disc posteriorly becomes excessive and the protrusion occurs.

A review of the literature has revealed no cases wherein the precipitating trauma has been electrical in nature. The effects of accidental electrical shocks upon the various tissues have been cited,[7 8 9] but there has been no report of such shocks causing protrusion of the intervertebral discs. A study of electro-convulsive therapy reveals no cases of protruded intervertebral disc due to either the electrical shock or the subsequent convulsion.[10 11 12] Likewise a study of the literature on insulin and metrazol shock therapy has shown no case of protruded disc secondary to convulsion.

Case History.—This thirty-five-year-old white man, who had been previously well with no history of preceding trauma or of any low back or leg pain, says that on August 7, 1946, while working on his tractor, he came in contact with a wire carrying a current of 6,900 volts. He immediately became unconscious so that he has no memory of a convulsion. Eye witnesses say that there was no convulsion, although there was a flexion of the body. He remained semi-conscious for fifteen hours. When he awakened he suffered from burns on his right foot which eventually healed under local treatment. Two days following this near electrocution, however, he began to complain of sharp, shooting pain in the left leg which became progressively severe.

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The pain radiated from the low back, down the left hip and down the posterior aspect of the left leg. The pain was made worse by coughing or sneezing or by having a bowel movement. The pain was worse in the morning and would awaken him from sleep at night. He also complained of low back pain which was constant and made worse by motion.

Complete physical examination was essentially negative with the exception of a scar on the right foot due to the burn. Neurologic examination was negative with the exception of the following positive findings. He had a muscle spasm of the lumbar paravertebral muscles with a loss of the lumbar curve. He had a list to the right. Upon palpation and percussion he had a tender area between L4 and 5 just to the left of the midline. He has a positive Lasegue's sign (straight leg raising sign) on the left, a tender sciatic nerve and an area of hypo-esthesia to pin prick and cotton wool corresponding to the skin segments of L4 on the left side. The reflexes were all present and equal.

The diagnosis was made of a protruded intervertebral disc between L4 and 5. He was operated upon at West End Baptist Hospital on October 25, 1946.

Operative Report.—Under local novocaine-sodium "pentothal" anesthesia a midline incision was made over the fourth and fifth lumbar spinous processes. The paravertebral muscles were stripped subperiosteally from the laminae of L4, 5 and S1. The ligamentum flavum was excised between the interspaces of L4 and 5 and L5 and S1. Upon retraction of the fifth lumbar root and the dura mater medially at the interspace of L5 and S1 no protrusion of the intervertebral disc was felt and the interspace had a normal, hard, rubbery resistance which was interpreted as containing a healthy intervertebral disc. Our attention was then diverted to the suspected area between L4 and 5. Upon retraction of the nerve root and the dural sac medially, at this interspace, a large white glistening protrusion was noted which had compressed the fourth lumbar root and was adherent to it. The root was dissected free and the posterior longitudinal ligament was incised. The white pulpy nuclear material began to extrude and upon insertion of a forcep it could be ascertained that the annulus fibrosus was ruptured. Accordingly, a rongeur was inserted into the interspace and the entire intervertebral disc was removed in one piece. The interspace was then curetted so that all of the nuclear material was removed. Hemostasis was obtained and it could be seen that the fourth lumbar root was well decompressed and freely movable. The wound was closed in layers in the usual fashion. Pathologic examination of the disc revealed degeneration and occasional areas of diffuse old hemorrhages into the nucleus pulposus.

Postoperative Course.—The patient progressed nicely. His leg pain was gone upon awakening. He required no catheterization. The sutures were removed on the sixth day. He was allowed up on the seventh day and returned to his home on the eighth day free from leg pain and with only a residual minor low back pain, which was gone at the time of his first follow-up examination three weeks later. Periodic check-up visits have revealed that the leg pain has remained absent. He has an occasional low back pain which he passes off as of no consequence. This pain was absent at the time of the last examination on January 15, 1947.

SUMMARY

A patient suffering from a protruded intervertebral disc apparently caused by an electrical shock has been reported. No similar cases have been found in a search of the literature.

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STREPTOMYCIN IN URINARY INFECTIONS

The latest edition of Cushny[1] lists penicillin as the most useful of the antibiotics and streptomycin as next. Variables which influence their effectiveness are being rapidly investigated. One of the difficulties with streptomycin particularly is the speed with which micro-organisms originally susceptible become resistant to it. A survey of the effectiveness of this drug in urinary tract infections has recently been made by Harrell, Herndon, Gillikin and Aikawa,[2] of Bowman Gray School of Medicine. They consider it the most useful antiseptic for infections due to Gram-negative bacilli. The commonest cause of failure of treatment in their series was development of bacteria-fastness in organisms at first sensitive.

A minimum daily dose of 0.6 gram streptomycin was needed to assure an active blood level and urine concentration, and 0.8 gram was generally employed. More than half of their series of 52 urinary tract infections were rapidly sterilized under streptomycin treatment. Sometimes sterilization took place while the blood level remained low; sometimes therapy failed when blood streptomycin remained high. At times treatment succeeded when the infecting micro-organism was not susceptible to the drug *in vitro*, although parallelism of *in vivo* and *in vitro* susceptibilities was usual.

Fastness to the drug developed rapidly and was permanent. Repetition of therapy after drug fastness had appeared, was invariably unsuccessful.

Mixed infections frequently cleared, in which not all of the organisms were susceptible to streptomycin. The effectiveness of therapy was greatly decreased by the presence of a complication: a foreign body such as a cystostomy tube, urethral catheter or calculus, obstruction to urinary flow by hydronephrosis, neurogenic bladder paralysis or benign prostatic hypertrophy, or impaired renal function.

In the presence of complications the cases usually became drug resistant and remained so.

It was considered important to alkalinize the urine.

Of the cured cases, more than half were followed and determined to be free of infection six months later, although one had had an infection of twenty-two years standing.

Because of the speed with which resistance develops, perhaps streptomycin should be administered sparingly, after urologic study where possible. Other antiseptics might be tried first in the usual case, or streptomycin might be used briefly to clear a case for immediate investigation when this is needed.

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2. Harrell, George T.; Herndon, E. Garland, Jr.; Gillikin, Charles M.; and Aikawa, Jerry K.: A Bacteriologic Study of the Factors Affecting the Efficacy of Streptomycin Therapy of Urinary Tract Infections. J. Clin. Investig., 26:577 (May) 1947.

CLASSIFICATION OF RECENT ANTISEPTICS

The term, antibiotic, now very popular, is not well chosen. Literally translated it means merely "against life"; and it is employed with a very definite meaning not inherent in the Greek derivation. It is used to designate a small group of blood stream antiseptics derived from living processes of micro-organisms: penicillin from the mould, Penicillium notatum; streptomycin from the mould, Actinomyces griseus; other less popular earth or mould filtrates such as clavacin or tyrothricin, and presumably other substances to be derived in the future from fungal, bacterial, or protozoal growth.

Actually all antiseptics are antibiotic. The sulfonamides are as much "against life" as penicillin or streptomycin. They differ in being derived originally from non-living material. The bacteriophage is a filtrate of living matter which is also against life of another microbic species. Bichloride of mercury is against life, as are the metallic poisons and another group of substances of recent interest, the antivitamins.

Chemically the activity of the antibiotics and the sulfa drugs also, is believed to be similar to that of the antivitamin substances; they combine with a host product at a critical point in its metabolic processes, displacing an essential nutritive element.[1] In this sense pyrithiamine, the antivitamin for thiamine, is an antibiotic. Sulfanilamide is an antibiotic for bacteria which require para-amino benzoic acid; and it is also an antivitamin in this reaction.

The term antibiotic, however, doubtless will remain in usage until a better is supplied, perhaps until there is a complete reclassification and revision of nomenclature of pharmacology, which has sprawled out like a surprised mediaeval city over the prodigious modern sciences of nutrition, chemistry and bacteriology.

LOCAL PENICILLIN

Because the sulfonamides and the mould filtrates have a direct bactericidal action in a test tube as well as in the living animal, they have been at times variously employed as local antiseptics. In pure powder form one of these substances may be dusted into an operative wound, and has been, with the idea that it would be absorbed to some extent in the blood stream, and that certainly it would eliminate some of the infection and that it could do no harm. The powdered substances have been applied in the abdomen in peritonitis and in other infectious conditions.

It is a frequent practice, according to Fleming and Fish,[2] of London, in some localities, to use powdered penicillin in oral surgery. Particularly in apicectomy it may be introduced into the cavity after excision of the ends of a tooth root. If this operation is to succeed, it is very necessary that a firm blood clot establish itself in the root cavity. A marked tendency has been observed for the clot to break down in cases treated with powdered penicillin.

In order to analyze this result, the London workers studied the effect of penicillin upon blood clotting outside the body. Various dilutions of the drug in saline were added to normal human serum and the clotting time and serum formation were noted. The clot usually formed in two minutes in normal saline alone. Clotting in the presence of penicillin was often markedly delayed; even as little as 340 units per c. c. of saline had some retarding effect. Clotting in the presence of penicillin around 12,000 units per c. c. was delayed more than half an hour. In greater concentrations than this, no clot formed in twenty-four hours.

Penicillin powder dusted into a wound, say these authors, may introduce as much as ten thousand or more units of active substance. The drug was developed and studied, of course, chiefly as a blood stream antiseptic, and in the concentrations in which it is used parenterally it is harmless. In the much greater concentrations in which the powder may be applied locally, it may have a number of undesirable effects, one of which, the delay of blood clotting, they have thus demonstrated. Clot formation is important in any operation or accident in which blood is let.

Their findings have no bearing upon the systemic effects of penicillin, since the concentration ordinarily obtained in the blood stream is in the region of only one unit per c. c. or less. Local use in an operation where formation of a blood clot is of importance, they suggest, should be limited to washing out the cavity with a solution of the drug not exceeding 100 units per c. c. This may be combined with intramuscular injections if there is reason to fear wound infection by penicillin-sensitive organisms.

This advice from Sir Alexander Fleming, discoverer of the most used antibiotic,[3] is well worthy of attention. The suggestion for local use of penicillin solution at 100 units per c. c. may have several practical applications.

1. Current Comment: Antivitamin Activity of Related Compounds. J.A.M.A., **134**:1550 (Aug. 30) 1947.

2. Fleming, Alexander; and Fish, E. W.: Influence of Penicillin on the Coagulation of the Blood, with Especial Reference to Certain Dental Operations. Brit. M. J., p. 242 (Aug. 16) 1947.

3. Fleming, Alexander: Brit. J. Exper. Path., **10**:226, 1929.

INTERNATIONAL CONGRESS ON TROPICAL MEDICINE AND MALARIA

Nowadays when United States foreign policy is more important to every citizen than anything it can do domestically, an international gathering of scientists is particularly important. It offers another much needed opportunity to promote friendliness and understanding among educated persons of different nationalities.

A fourth International Congress on Tropical Medicine and Malaria will meet in Washington in May 1948 under the sponsorship of the Department of State. Over sixty governments have been invited to take part.

The Southern Medical Association joined with the American Society of Tropical Medicine, the National Malaria Society and other interested groups in asking the Department of State to sponsor this Congress.

TWENTY-FIVE YEARS AGO

From Journals of 1922

Pancreatic Hormone in Diabetes.[1]—Less than half a century has elapsed since the pregnant discovery by von Mering and Minkowski in 1889 of the highly important part which the pancreatic gland plays in the control of carbohydrate metabolism in the body. Their classic experiments demonstrated that if the pancreas is completely extirpated, hyperglycemia, glycosuria, and the complete loss of the power to burn glucose or other carbohydrate ensues. There have been numerous attempts to supply this missing "regulator" of sugar metabolism * * * The latest experiments by the Toronto workers bring the significant evidence that injections of the substance isolated lower the content of sugar in the blood of normal animals as well as those rendered diabetic * * * the pancreatic factor does not * * * influence the glycolytic power of blood *in vitro* * * * is exerted in the active tissues themselves * * * The investigators are wisely withholding the product from general use while it is undergoing thorough trial * * * the history of medicine warns against haste in acceptance of "specifics."

Right Handedness and Left Handedness among Prehistoric Men.[2]—The scientist Sarafin examined sometime ago a number of implements from the oldest and the most recent periods of the Stone Age * * * The investigation, which took various prehistoric implements into account, revealed the fact that men of the older and also of the more recent Stone Age worked with both hands almost indiscriminately. At the beginning of the age of bronze, however, a very sudden departure from the ancient habit is noticeable, for now almost all work is done with the right hand * * * Sarafin assumes that religious motives which possibly ascribed a baser significance to the left hand, restricted its use, just as today popular superstition regards the left hand as emblematic of evil.

Antivivisection Laws.[3]—At the polls in November in California, Colorado, and Washington, scientific medicine will be tried at the bar of public opinion * * * the people will decide by popular vote whether medical research involving the use of living animals shall be prevented. The antivivisectionists in these states, mistrusting or despising their legislature, are seeking through the initiative to bring about enactment of such measures by playing on the ignorance and the emotions of the people. No properly informed persons can vote in favor of the antivivisectionist measures proposed. In Washington * * * the foes of scientific medicine procured the passage of an act in 1921 granting to parents the privilege of forbidding examination of their children in school by the health authorities.

1. Editorial: A Pancreatic Hormone in Diabetes. J.A.M.A., 79:1428 (Oct. 21) 1922.

2. Berlin Correspondent: Right Handedness and Left Handedness among Prehistoric Men. J.A.M.A., 79:1442 (Oct. 21) 1947.

3. Editorial: Protecting Scientific Research at the Polls. J.A.M.A., 79:1520 (Oct. 28) 1922.

Book Reviews

Practical Dermatology and Syphilis. By Harry M. Robinson, M.D., Professor of Dermatology and Director of the Syphilis Department, University of Maryland, School of Medicine; Dispensary Physician, Out-Patient Department, Syphilis Division, Johns Hopkins Hospital. 582 pages and over 600 illustrations. Baltimore: Chelsea Publishing Company, 1947. Price $5.00 postpaid.

This unusual dermatology is designed for practitioners and not dermatologists. It is essentially clinical. Each disease discussed begins with "Sites of Predilection," which is a great aid in classifying the lesion for diagnosis.

By far the longest discussion is on syphilis, which covers 59 pages and is excellently done. The book is only the size of a small novel, and is richly supplied with photographs, over 600 of them, well selected and unusually clear. Various tables deal with the frequency of different skin diseases. There is a table for the Negro alone.

The frequency of skin diseases is so great that the general practitioner will welcome a little volume on them designed solely for him. It is preeminently suited for a desk reference book.

The American Illustrated Medical Dictionary. By W. A. Newman Dorland, A.M., M.D., F.A.C.S., Lieut. Col., M.R.C., U. S. Army; Member Committee on Nomenclature and Classification of Diseases of the A.M.A.; Editor of "American Pocket Medical Dictionary." 21st edition. 1660 pages, with 880 illustrations, including 233 portraits. With the collaboration of E. C. L. Miller, M.D., Medical College of Virginia. Philadelphia: W. B. Saunders Company, 1947. Price $8.00 without thumb index; $8.50 with thumb index.

This popular work continues to increase the number of new words made necessary by the steady advance of medicine and its applied branches of science. As formerly in the Twentieth Edition the spelling, pronunciation and meaning of words are given. Generous in tables and accessory data, the new Dorland like its predecessors, will be a much-thumbed book.

Medical vocabulary is a constantly changing thing, from one year to another, and an up-to-date dictionary a large instrument in keeping one's practice modern.

Atlas of Cardiovascular Diseases. By Irving J. Treiger, M.D., Assistant Professor of Medicine, University of Illinois, Chicago. 180 pages with 244 illustrations, 11 in color. St. Louis: The C. V. Mosby Company, 1947. Price $10.00.

Dr. Treiger's book is an attempt to present the essentials of cardiovascular disease in pictures. The reproductions of x-rays are enlightening but the photographs of gross pathological specimens are confusing and often unintelligible.

The commentary upon the pictures is often an oversimplification of facts told in over-complicated language. For example, on page 29 the author states: "Auricular fibrillation per se is not a sign of left or right ventricular failure. It is only an abnormal auricular rhythm and may be associated with a ventricular rate, which is slow, normal, or fast. The fast rate, unless it is paroxysmal, is evidence of ventricular failure and must be treated accordingly with digitalis." On page 169, he states: "The rupture of the interventricular septum may heal without any ill effect, leaving an opening in the septum."

A Manual of Fractures and Dislocations. By Barbara Bartlett Stimson, A.B., M.D., Med.Sc.D., F.A.C.S., Assistant Professor of Clinical Orthopedic Surgery, College of Physicians and Surgeons, Columbia University, New York City. Second edition. 223 pages with illustrations. Philadelphia: Lea & Febiger, 1947. Price $3.25.

This second edition does not enlarge the scope of fracture treatment but the changes in treatment of certain fractures brought about by the experiences of World War II and the increasing interest of civilian surgeons in recent years have been added. No elaborate technics or detailed operative procedures are included but all fractures of the trunk and extremities are adequately covered.

The book will serve as an up-to-date guide to the wealth of material that is published in texts and articles which frequently bewilder the student with their mass of detail. It is an excellently organized guide to the principles involved generally in the treatment of fractures and dislocations and to the general nature of the methods used in applying those principles to specific lesions.

Medical students and general practitioners will find this to be an extremely valuable handbook. It simplifies the fundamental facts without the burden of the detailed information demanded of the expert.

Nutritional and Vitamin Therapy in General Practice. By Edgar S. Gordon, M.D., Ph.D., Associate Professor of Medicine, University of Wisconsin. Third Edition. 410 pages. Chicago, Ill.: Year Book Publishers, 1946. Price $2.75.

In this volume, the author attempts to integrate the newer with the older information on nutrition. Without getting lost in technical detail the author covers the subject satisfactorily.

Among newer developments to which the author gives consideration is the role of certain of the B vitamins, folic acid, pantothenic acid, biotin, cholines and inositol in nutrition.

In way of criticism, one could ask for a more carefully denoted bibliography as authority for much of the experimental work that is summarized. In addition the book would be a better reference if its divisions were clearer.

A Textbook of Medicine. Edited by Russell L. Cecil, A.B., M.D., Sc.D., Professor of Clinical Medicine, Cornell University Medical College, New York City. With assistance of Walsh McDermott, M.D., Associate Professor of Medicine, Cornell University Medical College. Associate Editor for Diseases of the Nervous System: Harold G. Wolff, M.D., Associate Professor of Neurology, Cornell University Medical College. Seventh Edition. 1,730 pages, with 244 illustrations. Philadelphia and London: W. B. Saunders Company, 1947. Price $10.00.

Dr. Cecil has edited a seventh edition of his Textbook of Medicine, which varies from the sixth edition only in detail; the format, organization of material, and illustrations are essentially the same.

Some new material has been added, notably a discussion of headache, by Dr. Harold G. Wolff, which should serve as a useful reference. Penicillin and streptomycin are given due consideration in the treatment of various infections.

It is believed that the 167 contributors and the editor have made a seventh edition which will maintain the important place previous editions have reached among textbooks of medicine.

Southern Medical News

SOUTHERN REGIONAL CONFERENCE

A Southern Regional Conference, arranged by the Council on Medical Service of the American Medical Association, will be held at the Academy of Medicine, 875 Peachtree Street, N.E., Atlanta, Georgia, October 3, 8:30 a.m. to 4:00 p.m. There will be a luncheon at 1:00 o'clock at the Biltmore Hotel, Dr. Edgar H. Green, Atlanta, President-Elect, Medical Association of Georgia, presiding. The states participating are: Alabama, Florida, Mississippi, Tennessee and Virginia.

OKLAHOMA CITY CLINICAL SOCIETY

Oklahoma City Clinical Society will hold its seventeenth annual conference in Oklahoma City, Oklahoma, October 27-30. Registration fee of $15.00 includes Round Table Luncheons, Smoker, Clinical Pathological Conference, General Assemblies, Postgraduate Courses, Dinner Meetings, and Commercial Exhibits. For further information, address Executive Secretary, 512 Medical Arts Building, Oklahoma City, Oklahoma.

SEMINAR, AMERICAN CANCER SOCIETY, FLORIDA DIVISION

An educational seminar, under the auspices of the American Cancer Division, Florida Division, and staged by the Tumor Clinic of the Duval County Hospital, Jacksonville, Florida, will be held in the Auditorium of the Roosevelt Hotel, Jacksonville, Florida, November 12-14. The seminar will cover the entire field of malignant diseases. It is the first meeting of this nature to be held in this part of the country, and an invitation is extended to all physicians. Details of the meeting may be obtained from Dr. W. C. Sumner, Director, The Tumor Clinic of Duval County Hospital, 2000 Jefferson Street, Jacksonville 6, Florida.

ALABAMA

Southern Psychiatric Association will hold its annual meeting in Birmingham, October 13-14. Dr. Newdigate M. Owensby, Medical Arts Building, Atlanta, Georgia, is Secretary.

Dr. H. Earle Conwell, Associate Professor, Orthopedic Surgery, Medical School, University of Alabama, Birmingham, has been appointed one of the fifteen orthopedic surgeons in the United States by the Council on Medical Education of the American Medical Association to inspect certain medical areas with reference to their facilities for Post-Graduate Training of Orthopedic Surgeons. Dr. Conwell will inspect the area of Boston and its environs. Dr. Paul Colonna of Pennsylvania has been appointed for similar inspection in Alabama.

Dr. George L. Johnson, Thomasville, Georgia, has been appointed Chief Medical Officer of the Alabama Regional Office, Veterans Administration Hospital, succeeding Dr. Harley B. Fisk, who has been transferred to the Miami, Florida, Regional Office. Dr. Johnson was formerly Manager, Veterans Administration Hospital, Tuscaloosa, and recently on the staff of the Veterans Administration Hospital at Thomasville, Georgia.

Deaths

Dr. Albert Russell Stephens, Delta, aged 89, died recently.

Dr. Arthur Edward Wilks, Birmingham, aged 61, died September 6.

ARKANSAS

Dr. Henry C. Chenault, Dean, University of Arkansas School of Medicine, Little Rock, has been made Vice President of the University in charge of medical education and hospitalization.

Dr. Benjamin B. Wells, formerly Associate Professor of Medicine, University of Arkansas School of Medicine, Little Rock, has been appointed Dean of the Medical School.

University of Arkansas School of Medicine, Little Rock, will have as full-time head of Department of Radiology Dr. Isadore Meschan, former Instructor of Radiology, Western Reserve University School of Medicine, Cleveland, Ohio; and as full-time head of the Department of Pediatrics Dr. William A. Reilly, former Associate Professor of Pediatrics, University of California Medical School, Berkeley-San Francisco.

DISTRICT OF COLUMBIA

George Washington University Medical Society at its recent annual business meeting installed Dr. Clyde P. Reeves, President; and elected Dr. James I. Boyd, President-Elect; Dr. Herbert S. Gates, First Vice President; Dr. Carolyn Pincock, Second Vice President; and Dr. Oscar B. Hunter, Secretary-Treasurer.

Medical Society of the District of Columbia will hold its next meeting at Washington, October 6-8.

Louis Mackall Medical Society has elected Dr. Walter Atkinson, President; Dr. Leo B. Gaffney, Vice President; and Dr. J. Lawn Thompson, Secretary-Treasurer.

Dr. Winfred Overholser, Washington, recently took office as the new President of the American Psychiatric Association at its 103rd annual meeting held in New York City.

Dr. William A. Morgan, Washington, is the Executive Secretary of an Advisory Committee to undertake surveys of health problems in the territories and island possessions of the United States.

Washington Gynecological Society has elected Dr. William J. Cusack, President; Dr. Jacob Kotz, Vice President; Dr. Herbert P. Ramsey, Secretary; Dr. George Nordlinger, Treasurer; and Dr. David H. Kushner, Historian.

Washington Ophthalmological Society has elected Dr. Edward J. Cummings, President; Dr. Jerome A. Sansoucy, Vice President; and Dr. John T. Schnebly, Secretary-Treasurer.

Dr. Shelley U. Marietta, Major General, retired, Washington, was elected President of the American College of Chest Physicians at its recent annual meeting.

Dr. Clifford James Tichenor, Washington, and Miss Irene Mathilda Kruka were married recently.

Deaths

Dr. Harry Theodore Harding, Washington, aged 77, died recently of diabetes mellitus.

Dr. Wilhelm Edmund Harman Krechting, Washington, aged 69, died recently of cerebral hemorrhage.

Dr. Courtney M. Smith, Washington, aged 43, was killed recently in an airplane crash.

Dr. Benjamin F. Iden, Washington, aged 64, died July 6.

FLORIDA

Miami Obstetrical and Gynecological Society was organized November 14, 1946, with Dr. M. C. Wilson as President. At the May 1947 meeting the following officers were elected for the ensuing year: Dr. Robert T. Spicer, President; Dr. Homer L. Pearson, Vice President; Dr. Ralph W. Jack, Secretary; and Dr. Norman McLeod, Treasurer.

Dr. J. Randolph Perdue, Miami, has been elected President, South Atlantic Association of Obstetrics and Gynecology, this Association covering Virginia, North Carolina, South Carolina, Georgia and Florida.

Dr. Leldon W. Martin, Sebring, and Miss Clara Sheperd, Fairmount, Georgia, were married recently.

Dr. Benjamin F. Oren and Dr. Martin S. Belle announce their association in the practice of internal medicine and gastroenterology in the duPont Building, Miami.

Dr. Jerome Karmiol, Chief Medical Officer, Regional Office, Veterans Administration, Miami, has resigned to enter private practice.

Deaths

Dr. Everton Jay Lawrence, Windermere, aged 70, died recently of hypertension and heart disease.

Dr. Howard Simmons Paine, Miami, aged 90, died recently of pneumonia.

GEORGIA

Georgia Public Health Association recently installed Dr. M. E. Winchester, Brunswick, President; and elected Dr. Clair A. Henderson, Savannah, President-Elect; Mr. W. A. Willman, Sanitation Engineer, *Columbus-Muscogee County Health Department, Vice President; and Miss Lova G. Lenert, State Department of Public Health, Secretary-Treasurer, reelected.

Polk General Hospital, Cedartown, providing twenty-six beds for white patients and six for colored patients, was recently completed. Dr. P. O. Chaudron, Cedartown, is Chief of the Medical Staff.

Dr. James A. Redfearn, Albany, recently received the highest recognition accorded by the University of Georgia Alumni Society, the award for outstanding services to his Alma Mater.

Dr. Walter A. Norton, Savannah, a fellow in the American College of Surgeons, was recently chosen a senior fellow in the Southeastern Surgical Congress.

Dr. Buford L. O'Neal, Atlanta, is associated with Dr. Herschel

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ANNOUNCING THE SEVENTEENTH ANNUAL CONFERENCE OF THE OKLAHOMA CITY CLINICAL SOCIETY

October 27, 28, 29 and 30, 1947

DISTINGUISHED GUEST LECTURERS

Edward Allen, M.D., GYNECOLOGY, University of Illinois School of Medicine, Chicago, Illinois.

William Arthur Altemeier, M.D., SURGERY, College of Medicine, University of Cincinnati, Cincinnati, Ohio.

Carl E. Badgley, M.D., ORTHOPEDIC SURGERY, University of Michigan School of Medicine, Ann Arbor, Michigan.

Edward L. Bortz, M.D., President of the American Medical Association, Philadelphia, Pennsylvania.

A. Carlton Ernstene, M.D., MEDICINE, Cleveland Clinic, Cleveland, Ohio.

Wiley Davis Forbus, M.D., PATHOLOGY, Duke University of Medicine, Durham, North Carolina.

Thomas E. Jones, M.D., SURGERY, Surgical Division, Cleveland Clinic, Cleveland, Ohio.

H. Dabney Kerr, M.D., X-RAY THERAPY, College of Medicine University of Iowa, Iowa City, Iowa.

Linwood D. Keyser, M.D., UROLOGY, Roanoke Hospital, Roanoke, Virginia.

Edward Lacy King, M.D., OBSTETRICS, Tulane University School of Medicine, New Orleans, Louisiana.

Frank D. Lathrop, M.D., OTOLARYNGOLOGY, Lahey Clinic, Boston, Massachusetts.

George M. Lewis, M.D., DERMATOLOGY, Cornell University School of Medicine, New York City, New York.

Samuel F. Marshall, M.D., SURGERY, Lahey Clinic, Boston, Massachusetts.

Herbert C. Miller, M.D., PEDIATRICS, University of Kansas School of Medicine, Kansas City, Kansas.

Edith L. Potter, M.D., PATHOLOGY, University of Chicago School of Medicine, Chicago Lying-In Hospital, Chicago, Illinois.

C. Wilbur Rucker, M.D., OPHTHALMOLOGY, Mayo Foundation, Graduate School of the University of Minnesota.

Cyrus C. Sturgis, M.D., MEDICINE, University of Michigan School of Medicine, Ann Arbor, Michigan.

Elmer G. Wakefield, M.D., MEDICINE, Mayo Foundation, Graduate School of University of Minnesota.

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Smoker **General Assemblies** **Commercial Exhibits**
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Registration fee of $15.00 includes all the above features

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Continued from page 880

C. Crawford in the Doctors Building, practice limited to diseases of the eye, ear, nose and throat.

Dr. C. C. Chappel, Jr., recently released from military service, is taking over the offices of Dr. W. V. Roberts, Lumpkin. Dr. Roberts has joined the staff of a hospital in Jacksonville, Florida.

Dr. William E. Carskadon, Atlanta, is associated with the Lowance Clinic in the Doctors Building.

Dr. T. M. Cole, formerly of Newnan and a graduate of the University of Edinburgh, Scotland, School of Medicine, has opened offices in the Doctors Building, Albany, for the practice of medicine.

Dr. O. F. Deen, formerly of Douglas, is associated with Dr. W. P. Kirkland, Manchester, for the practice of medicine.

Dr. Joseph M. Jackson, Waycross, is associated with Dr. W. R. McCoy, Folkston, at McCoy Hospital, for the general practice of medicine.

Dr. Joe S. Robinson, formerly of Rochelle, is associated with Dr. J. I. Matthews, Matthews Hospital, Dallas, for the practice of medicine and surgery.

Dr. W. G. Watson, formerly of Trenton, South Carolina, and recently released from military service, is associated with Dr. J. W. Thurmond, Augusta, for the practice of medicine.

Dr. John D. Wiley, Sparta, has moved to Morganton, North Carolina, where he is connected with one of the state mental hospitals.

Dr. A. H. Frye, Jr., Griffin, succeeds Dr. T. G. Smaha, Griffin, resigned, as Central of Georgia Railroad Surgeon for Griffin.

Dr. Herbert L. Treusch, Atlanta, has been promoted to the consulting staff of the Board of Veterans Appeals, Washington, D. C.

Dr. Marion C. Pruitt, Atlanta, has been promoted from Associate in Surgery, Emory University School of Medicine, to Assistant Professor of Clinical Surgery (Proctology).

Deaths

Dr. James Andrew Fountain, Macon, aged 54, died recently of a heart attack.

Dr. Marcus Lafayette Hickson, Fort Valley, aged 55, died recently of a heart attack.

Dr. Farish Clay Holden, Atlanta, aged 47, died July 15.

Dr. Gustavus T. Lyon, Roswell and Atlanta, aged 82, died July 1.

Dr. Charles Wesley Roberts, Atlanta, aged 64, died July 28 of a heart attack

Dr. Henry Cliff Sauls, Atlanta, aged 60, died July 15.

KENTUCKY

Dr. Ray H. Vanderhook has been assigned Chief of the Surgical Service at the U. S. Public Health Service Hospital, Lexington.

Dr. Fred Oesterle, formerly Chief of the Surgical Service at the U. S. Public Health Service Hospital, Lexington, has been assigned to the Marine Hospital, Staten Island, New York, to take post-graduate work in surgery.

Dr. J. B. Floyd, formerly Director of the tuberculosis prevention work with the Kentucky State Health Service, is Chief Medical Director for Eastern Kentucky, Veterans Administration, with headquarters at Lexington.

Deaths

Dr. Benjamin G. Argabrite, Greenville, aged 71, died recently of coronary thrombosis

Dr. William Calvin Crowell, Jr., Maysville, aged 29, was killed in an automobile accident recently.

Dr. Owen M. Carroll, New Castle, aged 76, died recently of pneumonia and cardiac decompensation.

Dr. Dell S. Edwards, Covington, aged 90, died recently of heart disease.

Dr. Charles M. Eckler, Williamstown, aged 67, died recently of heart disease.

Dr. Duke Marvin Godbey, Perryville, aged 68, died recently of cerebral hemorrhage.

Dr. George Washington Morgan, Yerkes, aged 66, died recently.

Dr. William E. Sparks, Sandy Hook, aged 73, died recently.

Dr. Claude Milton Vaughan, Paris, aged 63, died recently of metastatic melanosarcoma.

LOUISIANA

A state branch of the American Academy of General Practice was organized in Alexandria, July 13, by the general practitioners of Louisiana, this being the first state to organize a chapter in this new nationwide organization. The following officers were elected: Dr. J. P. Sanders, Shreveport, President; Dr. Guy Jones, Lockport, President-Elect; Dr. D. B. Barber, Alexandria, Vice

Continued on page 64

THE 1947 EDITION OF

Practical Dermatology and Syphilis

By

HARRY M. ROBINSON, M. D.

Professor of Dermatology, University of Maryland, Medical School

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New and better illustrations (more than 800 in all), with present day therapy, and modern technics are woven into the proved system of handling clinical diagnosis according to the structure and distribution of lesions. A statement of etiology, diagnostic aids, and treatment completes each clinical story.

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The George Washington University School of Medicine

ANNOUNCES

THIRD ANNUAL SERIES OF INTENSIVE POSTGRADUATE COURSES

(1)	Ocular Surgery, Pathology and Orthoptics	January 19-23, 1948
(2)	Ophthalmology	January 26-30, 1948
(3)	Surgery of the Extremities	February 2-6, 1948
(4)	Abdominal Surgery	February 9-20, 1948
(5)	Psychiatry	February 16-27, 1948
(6)	Anesthesia	February 23-27, 1948
(7)	Neurology	March 1-5, 1948
(8)	Thoracic Surgery and Endoscopy	March 1-5, 1948
(9)	Thoracic Medicine	March 8-12, 1948
(10)	Gynecology	March 8-12, 1948
(11)	Infectious Diseases	March 15-19, 1948
(12)	Obstetrics	March 15-19, 1948
(13)	Metabolic Diseases	March 22-26, 1948
(14)	Newborn and Premature	March 22-26, 1948
(15)	Cardiovascular Diseases (including Electrocardiography)	March 29-April 9, 1948
(16)	Miscellaneous Topics: Recent Advances in Medicine	April 12-16, 1948

By appropriate combinations of the above, the following longer courses can be arranged:

Ophthalmology (courses #1, 2)	January 19-30, 1948
Surgery (courses #3, 4, 6, 8, 10)	February 2-March 12, 1948
Psychiatry and Neurology (courses #5, 7)	February 16-March 5, 1948
Internal Medicine (courses #7, 9, 11, 13, 15, 16)	March 1-April 16, 1948
Thoracic Diseases (courses #8, 9)	March 1-12, 1948
Obstetrics and Gynecology (courses #10, 12, 14)	March 8-26, 1948

(Other combinations can also be arranged)

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Washington 5, D. C.

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President; Dr. H. P. Forsyth, Alexandria, Secretary; and Dr. J. W. Atkinson, Gretna, Treasurer. Board of Directors: Dr. N. J. Chetta, New Orleans; Dr. Joel B. Gray, New Orleans; Dr. Philip Robichaux, Raceland; Dr. S. L. Gill, Shreveport; Dr. E. L. Carroll, Columbia; Dr. M. C. Wigginton, Hammond; Dr. O. W. Topp, Oberlin; and Dr. H. P. Forsyth, Alexandria.

Dr. Henry O. Colomb, New Orleans, has been appointed Professor of Psychiatry, Louisiana State University School of Medicine, New Orleans.

New Orleans Gynecological and Obstetrical Society at its recent meeting elected Dr. Earle Conway Smith, President; Dr. W. D. Beacham, President-Elect; Dr. Curtis H. Tyrone, Vice-President; Dr. John S. Herring, Secretary; and Dr. Harry Meyer, Treasurer.

Dr. John G. Snelling, Jr., Monroe, has been appointed Chairman of the Arrangements Committee for the Louisiana State Medical Society which meets in Monroe in 1948.

Dr. Morris Shaffer, Professor of Bacteriology, Tulane University School of Medicine, New Orleans, spent the summer in Jerusalem organizing a Basic Science Department at the University of Jerusalem and while there advised as to the establishment of a four year medical school.

Dr. Ralph H. Riggs, Shreveport, is one of fifty from a group of more than six hundred applicants who will take Dr. Samuel Fomon's course in rhinoplasty at the Manhattan General Hospital, New York City. This course is sponsored by the American Otorhinologic Society for the advancement of Plastic and Reconstructive Surgery.

Dr. Lewis E. Jarrett, Director of Touro Infirmary, New Orleans, resigned August 11.

Touro Infirmary, New Orleans, has a new X-Ray Department and a Tumor Clinic, which has just been completed.

Deaths

Dr. William Worthing Calhoun, New Orleans, aged 79, died recently.

Dr. Francis C. Bennett, Monroe, aged 77, died recently.

Dr. Guy Henry Faget, New Orleans, aged 56, died July 17.

Dr. Orren Pakenham Goodwin, Ruston, aged 56, died recently of heart disease.

Dr. Fred Houston Mecom, Columbia, aged 69, died recently of cerebral hemorrhage.

Dr. Joseph Tilford Scott, Sr., New Orleans, aged 78, died July 5 of a heart attack.

Dr. Paul West Winder, Shreveport, aged 42, died recently.

MARYLAND

The Board of Medical Examiners of Maryland recently issued licenses to practice in Maryland to 148 medical school graduates, 70 from University of Maryland, 43 from Johns Hopkins, nine from out of state medical schools and seven from foreign universities, the announcement being made by Dr. Lewis P. Gundry, Secretary of the Board.

Dr. Joseph F. Saduck, Jr., Baltimore, has been appointed Associate Medical Director to the home office staff of the Prudential Insurance Company of America.

Deaths

Dr. Frank Wheeler Hornbrook, Chevy Chase, aged 71, died recently.

Dr. Arthur John Lomas, Baltimore, aged 68, died recently.

Dr. Leander Burgess Milbourne, Baltimore, aged 67, died recently.

MISSISSIPPI

Dr. Robert L. Simmons, Meridian, recently became head of the Department of Preventive Medicine and Public Health, Louisiana State University School of Medicine, New Orleans. Dr. Simmons was formerly Director, Lauderdale County Health Department.

Deaths

Dr. Rufus Franklin Spears, Meridian, aged 60, died recently of chronic myocarditis and acute bronchitis.

Dr. John McElroy White, Jackson, aged 89, died recently of senility.

MISSOURI

Missouri Society for Neurology and Psychiatry will hold its annual fall meeting at the Glenwood Sanatorium, Webster Groves, October 14.

Dr. Millard F. Arbuckle, St. Louis, was elected President of the American Broncho-Esophagological Association at its recent annual meeting.

Dr. Cyrus E. Burford, St. Louis, was elected President of the Association of Genito-Urinary Surgeons of America at its recent annual meeting.

Continued on page 66

"Everything I Know About Him is Good..."

The writer of this letter went even further and stated that should he ever have to submit to surgery *personally*, he would choose our man. We don't think a greater compliment could be paid a young surgeon. He is the calibre of man you would want for an associate, assistant or resident.

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Continued from page 64

Dr. [illegible] M. Moore, Sr., Higginsville, has been appointed Physician at the Confederate Home, Higginsville.

Dr. A. N. [illegible], St. Louis, was installed President of the American Radium Society at its annual meeting held recently.

Dr. George H. Thiele, Kansas City, was installed President of the American Proctologic Society at its annual meeting held recently.

Dr. James Barrett Brown, St. Louis, has been awarded the Legion of Merit for his work as Chief of Plastic and Maxillofacial Surgery at Valley Forge General Hospital from June 1943 to August 1945.

Kansas City Southwest Clinical Society will hold its Annual Fall Clinical Conference at the Municipal Auditorium and Hotel President, Kansas City, October 6-9.

Missouri State Medical Board Examinations will be given October 20-22 in St. Louis.

Dr. William W. Stanbro, St. Louis, has been named Chief Roentgenologist at the George Washington University Hospital and Assistant Professor of Radiology of the George Washington University School of Medicine, Washington, D. C.

Excelsior Surgical Club, a national organization of surgeons who served in the Mediterranean Theater during World War II, will meet in St. Louis, October 17-18.

Dr. Lawrence T. Post, St. Louis, was awarded the Lucien Howe Medal of the American Ophthalmological Society in recognition of his work in teaching and leadership in study of eye diseases at the meeting of the Society held in Hot Springs, Virginia, in June.

Dr. Frederick A. Johansen, formerly of Kahoka, has been appointed Medical Officer in Charge, U. S. Marine Hospital, Carville, Louisiana.

DEATHS

Dr. Edwin Grey Cope, Hornersville, aged 65, died recently of heart disease.

Dr. James Edwin Dewey, Springfield, aged 67, died recently of coronory thrombosis.

Dr. Clyde Owen Donaldson, Kansas City, aged 69, died recently of cerebral occlusion.

Dr. William J. Loler, St. Louis, aged 71, died recently of cerebral hemorrhage.

Dr. Baxter Edward Morrow, Kansas City, aged 76, died recently.

Continued on page 68

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Bilirubin in Blood	Creatinine in Blood	pH of Blood	Urea in Urine
Blood Loss in Body Fluids	*Densiometer (Large)	pH of Urine	Uric Acid in Blood
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Continued from page 66

NORTH CAROLINA

Dr. Wingate Johnson, Winston-Salem, has been made a member of the Board of Trustees of the American Medical Association to succeed Dr. C. W. Roberts, Atlanta, Georgia, deceased.

American College of Physicians will hold its annual regional meeting in Chapel Hill, November 14.

Duke University School of Medicine has added to its Department of Medicine Dr. John Hickam, Dr. Frank L. Engel, and Dr. Jack D. Myers, all of Atlanta, Georgia.

The 1,000-bed hospital at Oteen, N. C., formerly an army general hospital, transferred to the U. S. Public Health Service and later to the Veterans Administration, is being used as a tuberculosis hospital by the Veteran's Administration, the original army buildings being replaced by permanent structures.

Dr. William A. Perlzweig, on a three months leave from duties as Professor of Biochemistry, Duke University School of Medicine, Durham, has been in Palestine as special advisor to the Hebrew University and the Hadassah Medical Organization in the proposed establishment of a Medical School at the University of Jerusalem.

Dr. William W. Hurteau, Davenport, Iowa, has been appointed an instructor in the Department of Pathology, Duke University School of Medicine, Durham.

A portrait of Dr. Wilburt C. Davison, Dean, Duke University School of Medicine, Durham, will be presented as a gift of the Medical Alumni to the School at the annual Fall Symposium, October 17-18.

Dr. H. Stuart Willis, Sanatorium, was elected Secretary of the National Tuberculosis Association at its meeting held recently in San Francisco.

Bowman Gray School of Medicine of Wake Forest College, Wake Forest, has been awarded to its various departments a total of $26,100 in research grants from the National Foundation for Infantile Paralysis, the John and Mary R. Markle Foundation, Life Insurance Medical Research Fund, and the Roche Memorial Foundation.

The addition of a sixth floor to the North Carolina Baptist Hospital, Winston-Salem, at an approximate cost of $85,000 including equipment, has been authorized and it is anticipated that it will be completed by late spring.

Dr. Wingate Johnson, Winston-Salem, has been named on a committee from the American Medical Association to study nursing needs in the United States.

Dr. W. C. Hunter, Wilson, has been elected Second Vice-President, Wilson County Tuberculosis Association.

Dr. Thomas Holt is associated with Dr. John Lane, Rocky Mount, in the practice of ophthalmology and otolaryngology.

Dr. J. T. Wyche, recently released from military service, is associated with Dr. R. C. Sadler, Whiteville, in the practice of medicine.

DEATHS

Dr. William Wilhelm Craven, Charlotte, aged 68, died recently of coronary thrombosis.

Dr. A. T. West, Durham, died September 13.

OKLAHOMA

Oklahoma Orthopedic Society was organized in Tulsa recently and elected Dr. Don O'Donoghue, Oklahoma City, President, Dr. Frank A. Stuart, Tulsa, Vice-President; and Dr. Samuel T. Moore, Oklahoma City, Secretary-Treasurer. To be eligible a physician must be a member of the American Board of Orthopedic Surgery. Two meetings will be held each year.

Dr. Charles E. Leonard and Dr. W. W. Rucks, Oklahoma City, have been named by the Governor to fill positions on the Mental Health Board.

Oklahoma Tuberculosis Association, at its recent annual meeting, elected Dr. George S. Baxter, Shawnee, President; Dr. Paul Stephenson, El Reno, and Dr. Oliver Hodges and Dr. Grady F. Mathews, both of Oklahoma City, Vice-Presidents; and Mrs. Paul Cress, Perry, Secretary.

Continued on page 70

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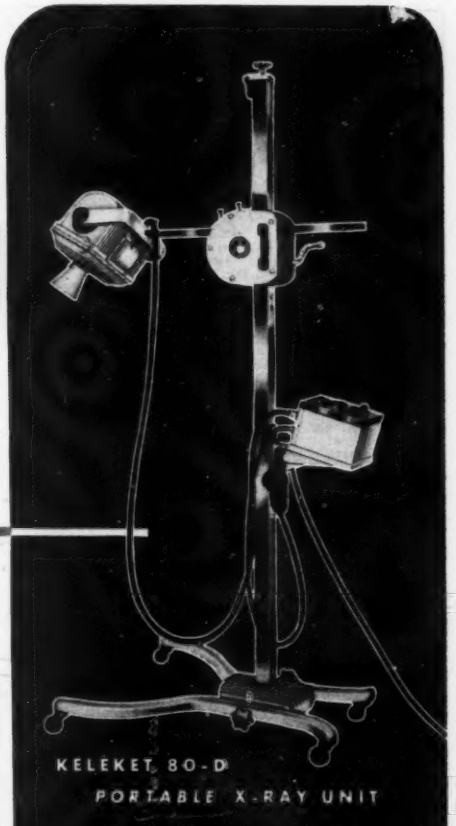

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Continued from page 68

Dr. Robert O. Ryan, formerly on the staff of the University of Oklahoma Student Health Service, has established a private practice at Norman.

Dr. Marvin S. Terrell is associated with Dr. R. V. Smith, Britton, in the practice of medicine. Dr. Smith recently completed his fiftieth year of service in the practice of medicine.

Dr. Fred W. Taylor, Oklahoma City, is on the staff of Weeks Hospital, Duncan.

Dr. Roy L. Fisher, for many years associated with the Frederick Clinic Hospital, Frederick, has returned to private practice in that city.

Dr. Harold E. Sanders, recently Chief of Dermatology, Alabama Regional Hospital, Fort McClellan, Alabama, is associated with the A. D. Smith Clinic, Stillwater.

Dr. C. E. Williams, Woodward, has returned from the World Jamboree of Boy Scouts in Moisson, France, which he attended as a physician on the central staff.

Dr. John G. Gilbert, formerly of Tulsa, is associated with Dr. R. B. Gibson, Ponca City.

Dr. Guy B. Van Sandt has reopened Wewoka Hospital, Wewoka, which has been closed two years.

Dr. N. C. Riley, Holdenville, is resident physician at Weeks Hospital, Duncan.

Dr. Fred P. Perry, Okeene, was recently elected President of the Board of Directors of the local Chamber of Commerce.

Deaths

Dr. Jesse A. Bates, Oklahoma City, aged 59, died recently.

Dr. David Wiggins Bennett, Sentinel, aged 75, died July 3 of a heart attack.

Dr. Robert LeRoy Browning, Pawnee, aged 64, died recently.

Dr. Galvin Luther Johnson, Pauls Valley, aged 67, died recently of heart disease.

Dr. Lee W. Cotton, Enid, aged 86, died recently.

Dr. George David Lewry, Hooker, aged 84, died recently.

Dr. James Samuel McFadin, Altus, aged 68, died recently.

Dr. William E. Simon, Alva, aged 60, died July 16.

Dr. George Reed Tabor, Tishomingo, aged 82, died recently of heart disease.

SOUTH CAROLINA

U. S. Naval Hospital is now under construction near Beaufort.

Dr. C. L. Guyton is head of a hospital division which has been established in the State Board of Health. Dr. Guyton was recently released from his duties as Greenville Health Commissioner, a position he assumed on May 1, to take full administrative charge of the hospital program.

Dr. John M. Pratt, Hickory Grove, has been appointed to the Board of Trustees of the Medical College of the State of South Carolina, succeeding the late Dr. J. R. DesPortes.

Dr. Keitt Smith has been elected to the Executive Committee of the State Board of Health to fill the vacancy created by the death of his father Dr. D. Lesesne Smith.

Dr. William H. Bridges, recently released from military service has opened an office in Columbia for the practice of neurological surgery.

Dr. Richard B. Ferguson, recently released from military service, has joined the staff of Veteran's Hospital, Columbia.

Deaths

Dr. Joe Hilliard Kirby, Jr., Loris, aged 29, died recently of acute leukemia.

Dr. Charles Henry Pate, Scranton, aged 67, died recently.

Dr. Samuel B. Moore, Spartanburg, aged 64, died recently.

Dr. Lewis Franklin Robinson, Greenville, aged 67, died recently.

TENNESSEE

Tennessee State Society of Pathologists was recently formed with Dr. Alfred Golden, Memphis, President; Dr. William A. DeMonbreun, Nashville, Vice-President; and Dr. Thomas C. Moss, Memphis, Secretary-Treasurer.

Dr. Cecil E. Newell, Chattanooga, announces the removal of his office to, and the opening of, The Cecil Newell Clinic, 407 East Fifth Street.

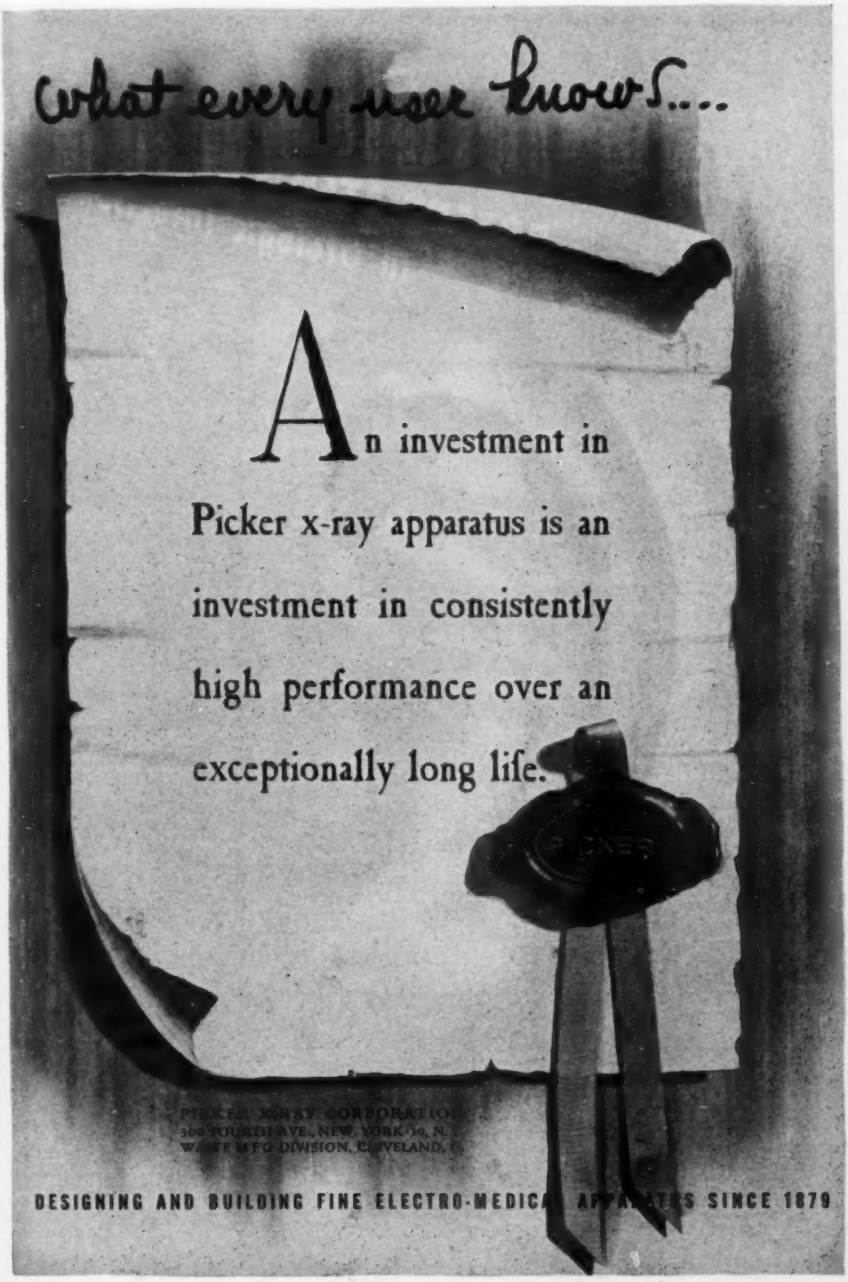
Dr. George F. Aycock, after thirty years with the Army Medical Corps, has returned to his native state to take up the direction of the tuberculosis program at the University of Tennessee Hospital, Knoxville.

Dr. Lawrence A. Grossman has opened his office in the Doctors Building, Nashville, for the practice of internal medicine.

Deaths

Dr. Henry Sidney Oaks, Rutledge, aged 63, died recently of cerebral hemorrhage and hypertension.

Continued on page 74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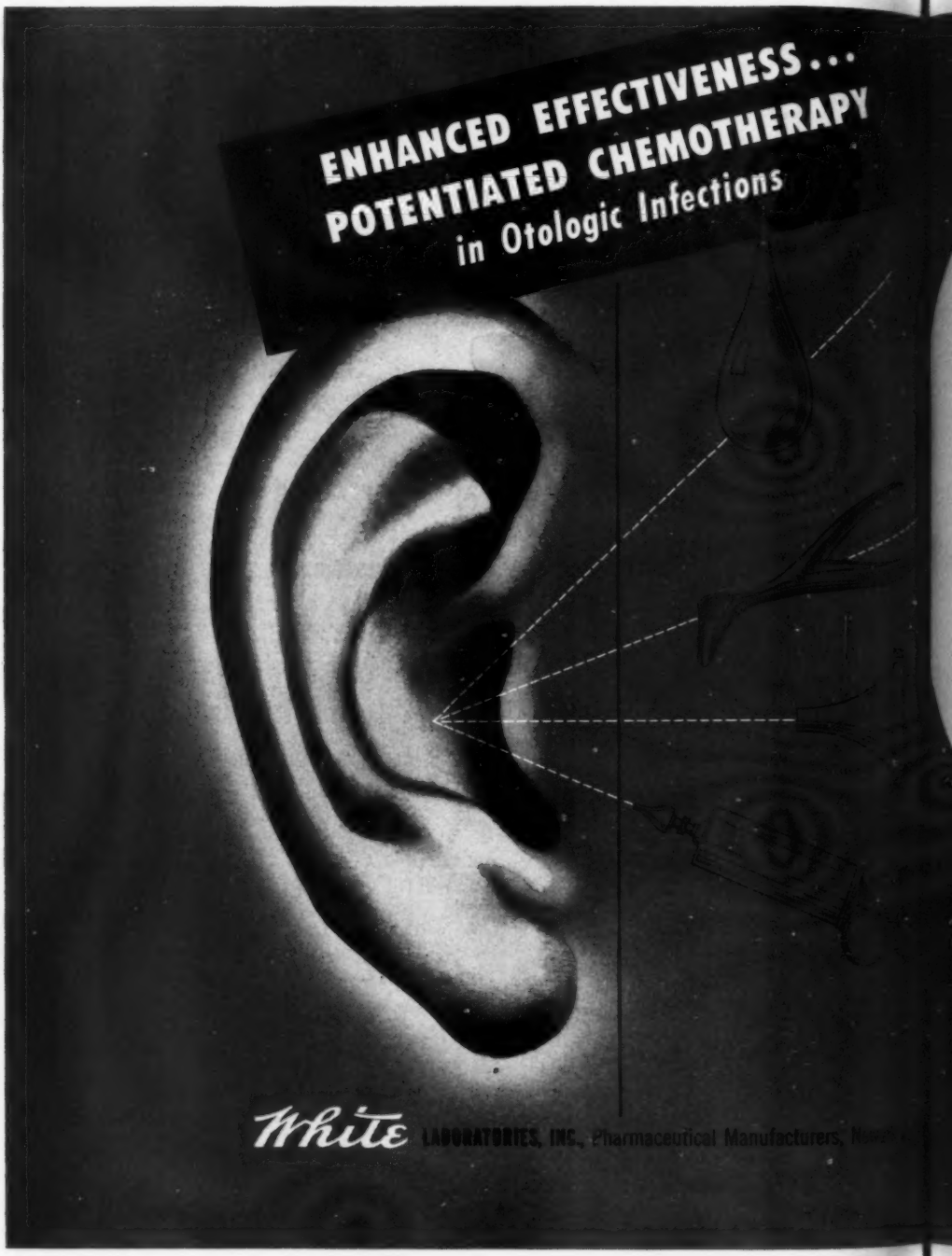
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Continued from page 70

TEXAS

Texas Association of Obstetricians and Gynecologists will hold its next meeting at Fort Worth, November 21-22, under the presidency of Dr. J. E. Kanatser, Wichita Falls.

Texas Society of Ophthalmology and Otolaryngology will hold its next meeting at Houston, December 5-6, under the presidency of Dr. W. E. Vandevere, El Paso.

University of Texas Medical Branch, Galveston, has received $3,000 from the Sugar Research Foundation, Incorporated, New York City, for the support of studies by Dr. W. A. Selle, Professor of Physiology, on protective factors in experimental cancer of the liver.

A memorial fund to honor the late Dr. A. O. Singleton, Professor of Surgery, has been created to support the work of the Department of Surgery, University of Texas Medical Branch, Galveston. Contributions may be sent to the Librarian, University of Texas Branch, Galveston.

Dr. C. T. Stone, Galveston, has been elected one of the Vice-Presidents of the American College of Physicians.

Dr. Robert M. Moore, Professor of Surgery, University of Texas Medical Branch, Galveston, has been named Chairman of the Department of Surgery.

Dr. Peel M. Payne, Asherton, and Mrs. W. L. Pilgreen, Uvalde, were married recently.

Dr. C. D. Bussey, Dallas, and Miss Lyda Lynn Wood, Waco, were married July 3.

Dr. Cecil Albert Johnson, Dallas, and Miss Marilyn Wyche, Overton, were married July 3.

DEATHS

Dr. James Crawford Anderson, Austin, aged 94, died recently.

Dr. Coral Ray Armentrout, Houston, aged 69, died recently.

Dr. John Andrew Lanius, Bonham, aged 75, died recently of arteriosclerotic heart disease and decompensation.

Dr. John Leslie Murphy, El Paso, aged 44, died recently.

Dr. Lorenzo Peyton McCuistion, Paris, aged 78, died July 16 of myasthenia gravis following eye operation.

Dr. Edward Lawrence Howard, Fort Worth, aged 70, died recently of coronary thrombosis.

Continued on page 76

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Continued from page 74

Dr. James Benjamin Granville, Brady, aged 66, died July 2 of heart disease.

Dr. Edward Jackson Burns, Bangs, aged 70, died recently of arteriosclerosis and heart disease.

Dr. John Thomas Harrington, Waco, aged 89, died recently.

Dr. Arthur Josephus Mynatt, Houston, aged 72, died recently of coronary thrombosis.

Dr. Albert Olin Singleton, Galveston, aged 65, died recently of coronary occlusion.

VIRGINIA

Twenty-First Annual Spring Graduate Course in Ophthalmology and Otolaryngology will be held at the Gill Memorial Eye, Ear and Throat Hospital, Roanoke, April 5-10, 1948.

Fauquier County Medical Society has elected Dr. V. L. McCullers, Remington, President; Dr. H. L. Townsend, Marshall, and Dr. Walter G. Trow, Warrenton, Vice-Presidents; and Dr. J. Frank Folk, Warrenton, Secretary-Treasurer.

Seaboard Medical Association of Virginia and North Carolina will hold its next annual meeting at The Cavalier Hotel, Virginia Beach, December 3-5. Dr. O. R. Yates, Suffolk, President, and Dr. Clarence Porter Jones, Sr., Newport News, Secretary.

Virginia Chapter, American College of Chest Physicians, at its recent annual meeting elected Dr. Dean B. Cole, Richmond, President; Dr. C. L. Harrell, Norfolk, Vice-President; and Dr. Charles W. Scott, Burkeville, Secretary-Treasurer.

Virginia Peninsula Health District has been divided into two units, the Elizabeth City-Warwick County Health District, Dr. Thomas F. McGough, Hilton Village, in charge; and the Charles City-James City-New Kent-York District, Dr. Linwood Farley, Williamsburg, Health Officer.

Continued on page 78

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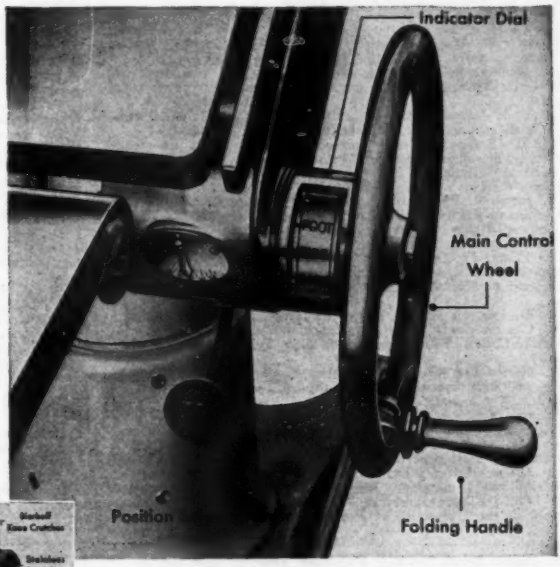

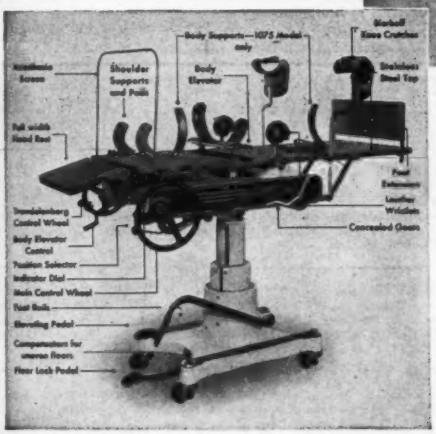

THIS superior Table features an INDICATOR DIAL and POSITION SELECTOR LEVER which permit the anesthetist—while remaining seated—to properly select the precise table position to correspond with the anatomical posture changes called for by the surgeon . . . or posture changes called for by the anesthetist for physiologic reasons.

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DESIGNERS AND MANUFACTURERS OF SURGICAL STERILIZERS, TABLES AND LIGHTS

Continued from page 76

Dr. George B. Tyler recently released from the Navy and now located at Staunton, succeeds Dr. Linwood Farley as Health Officer, Augusta County Health District.

Dr. Adney K. Sutthin, recently released from military service, is associated with Dr. Wyndham B. Blanton, Richmond, in the practice of internal medicine and allergy.

Dr. Wilbur M. Bowman, Petersburg, recently released from military service, has been appointed Health Officer of Petersburg, succeeding Dr. Mason Romaine, who resigned to become Director of Cancer Control of the State Health Department.

Dr. Kenneth J. Cherry is associated with Dr. Benjamin W. Rawles, Jr., Richmond, in the practice of general and gynecological surgery.

Dr. T. S. Jennings, Waverly, is now at Newton D. Baker Hospital, Martinsburg, West Virginia, as Chief of Tuberculosis.

Dr. F. G. Goodman has resigned as Instructor in the Duke University School of Medicine, Durham, North Carolina, and has returned to Wilmington for practice of internal medicine, allergy and hematology.

Dr. James C. Baker, Jr., has resigned as Director, Department of Continuation Education, Medical College of Virginia, Richmond, to become Medical Director, Greenbriar Clinic, White Sulphur Springs, West Virginia.

Dr. Frank F. Thweatt, Jr., Senior Surgeon with the U. S. Public Health Service, and a native of Petersburg, has been transferred to Norfolk to have charge of the U. S. Marine Hospital.

Dr. Rowland H. Walker, Martinsville, has moved to Norfolk.

Dr. Charles Henry Patterson, Lynchburg, and Mrs. Marguerita Goodricke-Cattell Young, Auckland, New Zealand, were married recently.

Dr. Martin Lee Rice, Jr., and Miss Virginia Lee Figg, both of Richmond, were married recently and will make their home in Memphis, Tennessee.

Dr. and Mrs. Rudolph W. Holmes, Charlottesville, formerly of Chicago, have presented their library, chiefly on obstetrics and gynecology, to the University of Virginia Medical Library, as a memorial to their respective mothers, Paula Wieser Holmes and Sarah Moore Baxter. Dr. Holmes formerly was Professor of Obstetrics and Gynecology, Rush Medical College, Chicago, and since 1926 Professor Emeritus, University of Chicago, and more recently of the University of Illinois.

Deaths

Dr. Carroll Harris Fowlkes, Richmond, aged 59, died July 6.

Dr. James Millard Graybeal, Marion, aged 70, died July 6.

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Dr. Hugh Page Newbill, Staunton, aged 38, died July 2.

West Virginia

West Virginia Heart Association will meet in Parkersburg, October 2.

West Virginia Public Health Association will hold its northern district fall meeting at Clarksburg, October 17, and its southern district fall meeting at Beckley, October 20.

Dr. R. P. Fosnaugh, Parkersburg, has been appointed part-time Health Officer for Wood County, succeeding Dr. C. E. Morehead, resigned.

Dr. A. G. Lanham, Ronceverte, has been reappointed part-time Health Officer of that city.

Dr. Roscoe Stotts, Kenova, has been reappointed Health Officer of that city.

Dr. Melford L. Hobbs, Fairmont, has been appointed Head Pathologist and Clinical Pathologist, West Virginia School of Medicine, succeeding Dr. C. C. Fenton.

Dr. John Q. Godbey, Sophia, has moved to Glen Daniels.

Dr. J. W. Calvert, Lamar, has moved to Lynwood, New York.

Dr. Robert G. Williamson, Jr., Madison, has moved to Marmet.

Dr. C. W. Shafer, Spencer, has accepted a two years residency in anesthesiology at the University of Maryland Hospital, Baltimore.

Dr. W. P. Hamilton, who moved from Chapmanville to Greenwich, Ohio, early in the year has relocated at Chapmanville.

Dr. Edward F. Reaser, Huntington, succeeded Dr. Charles T. Taylor, August 1, as Superintendent of Huntington State Hospital.

Dr. George W. Lyon, Huntington, has been added to the staff on the Veteran's Administration Department of Medicine and Surgery, Washington, D. C.

Deaths

Dr. Jesse L. Lambert, Franklin, aged 76, died recently of diabetes mellitus.

Dr. Joseph Halloch Moore, Huntington, aged 45, died August 3, of coronary occlusion.

Dr. Wyndham Bolling Robertson, Kearneysville, aged 72, died August 9, of heart disease.

Classified Advertisements

LOCATION WANTED: F. A. C. S., experienced general abdominal surgeon with orthopedic and urology background. At present Chief of Surgical Service at government hospital, W. W. II veteran. Desires surgical association with clinic, group or partnership. Available about November or December. PSG, care Southern Medical Journal.

WANTED: Interns and/or residents in a general, private hospital of 150 beds in the Southeast. Service to begin immediately or as soon as available. Approved by A. M. A. and A. C. S. Salary $132.00 a month and maintenance. IHS, care Southern Medical Journal.

WANTED: A practicing physician for office and field work. A splendid location. Five-room clinic, office. Town of 10,000. Two other physicians. Write or phone Daly Drug Co., Tarrant, Ala. Phone 52-2384.

RESIDENCY: Spartanburg General Hospital, 350 beds, desires second year men. Approved internship a prerequisite. Salary $200.00 per month with $300.00 bonus at end of 12 months. Address Mr. J. L. Rogers, Superintendent, Spartanburg, S. C.

WANTED: Two physicians interested in general practice to become associated with group clinic and small hospital. Would like one man that can do some ear, eye, nose and throat along with with general practice. Salary first year $700 per month with gas and oil furnished for use of automobile used in practice. MAR, care Southern Medical Journal.

FOR SALE: Unused but not needed items at cost. One operating table and attachments—$764.50; one stretcher with pads and knee straps—$110.50; one wall shelf stand—$110.00; one instrument table, 20x40—$64.50. CA, care Southern Medical Journal.

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It Can Happen Here

Example of severe rickets in a sunny clime.

LEST WE FORGET—we who are of the vitamin D era—severe rickets is not yet eradicated, and moderate and mild rickets are still prevalent. Here is a white child, supposedly well fed, if judged by weight alone, a farm child apparently living out of doors a good deal. This boy was reared in a state having a latitude between 37° and 42°, where the average amount of fall and winter sunshine is *equal to that in the major portion of the United States*. And yet such stigmata of rickets as *genu varum* and the quadratic head are plain evidence that rickets does occur under these conditions.

How much more likely, then, that rickets will develop among city-bred children who live under a smokepall for a large part of each year. True, vitamin D is more or less routinely prescribed nowadays for infants. But is the antiricketic routinely administered in the home? Does the child refuse it? Is it given in some unstandardized form, purchased from a false sense of economy because the physician did not specify the kind?

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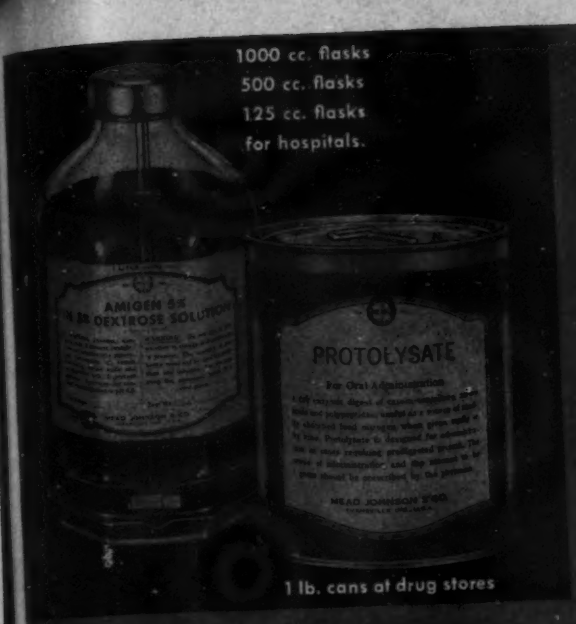

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Theelin in Oil in a 10 cc. multidose Steri-Vial®. Concentration: 1 mg. (10,000 units) per cc.

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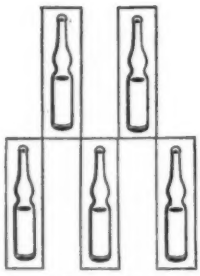
Aqueous Suspension of Theelin in 1 cc. ampoules containing 5 mg. (50,000 units). In packages of six and twenty-five ampoules each.



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